

Trisomy 18: Understanding Autoimmune Disorders



Antoine Demonceaux, MD, Elisa Song, MD, Youngran Chung, MD,
Robert c Dumont, MD



“DOCTORS ARE MEN WHO PRESCRIBE
MEDICINES OF WHICH THEY KNOW LITTLE,

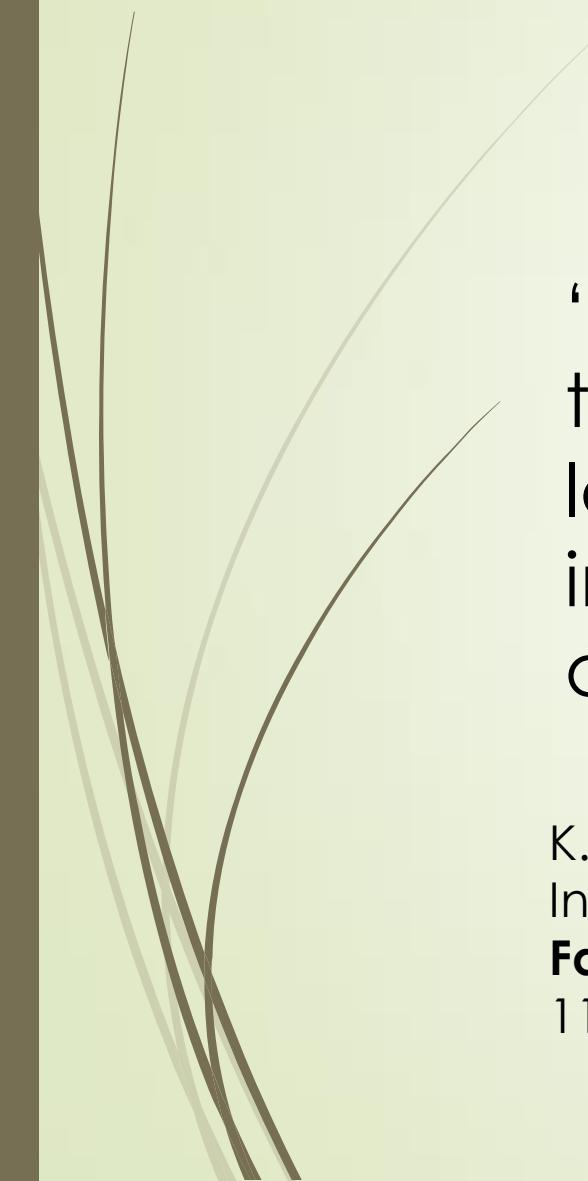
TO CURE DISEASES OF WHICH THEY KNOW
LESS,

IN HUMAN BEINGS OF WHOM THEY KNOW
NOTHING “

VOLTAIRE
1694-1778

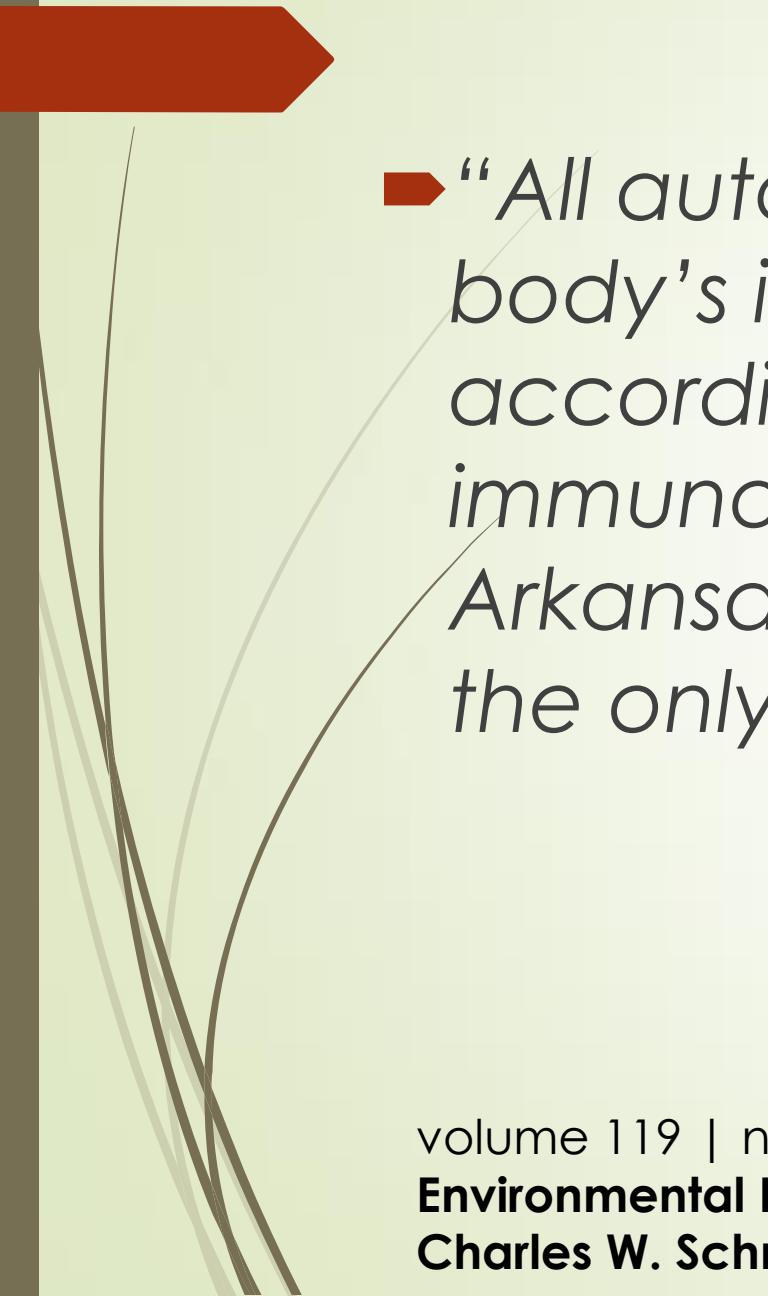


Understanding Autoimmune Disease



“The field is replete with competing theories and biological mechanisms, but it lacks a unifying concept”... “For every immunologist you’ll get one or two theories about what causes autoimmune disease,”

K. Michael Pollard, associate professor at The Scripps Research Institute. From: Environmental Health Perspectives **Environmental Factors in Autoimmune Disease Charles W. Schmidt**, MS volume 119 | number 6 | June 2011



► “All autoimmune diseases occur when the body’s immune system turns against itself. But according to Kathleen Gilbert, an immunologist and professor at the University of Arkansas for Medical Sciences, that’s about the only thing we know for sure about them.”

Autoimmune Disease: Definition



Autoimmune disease refer to problems with the acquired immune system's reactivity.

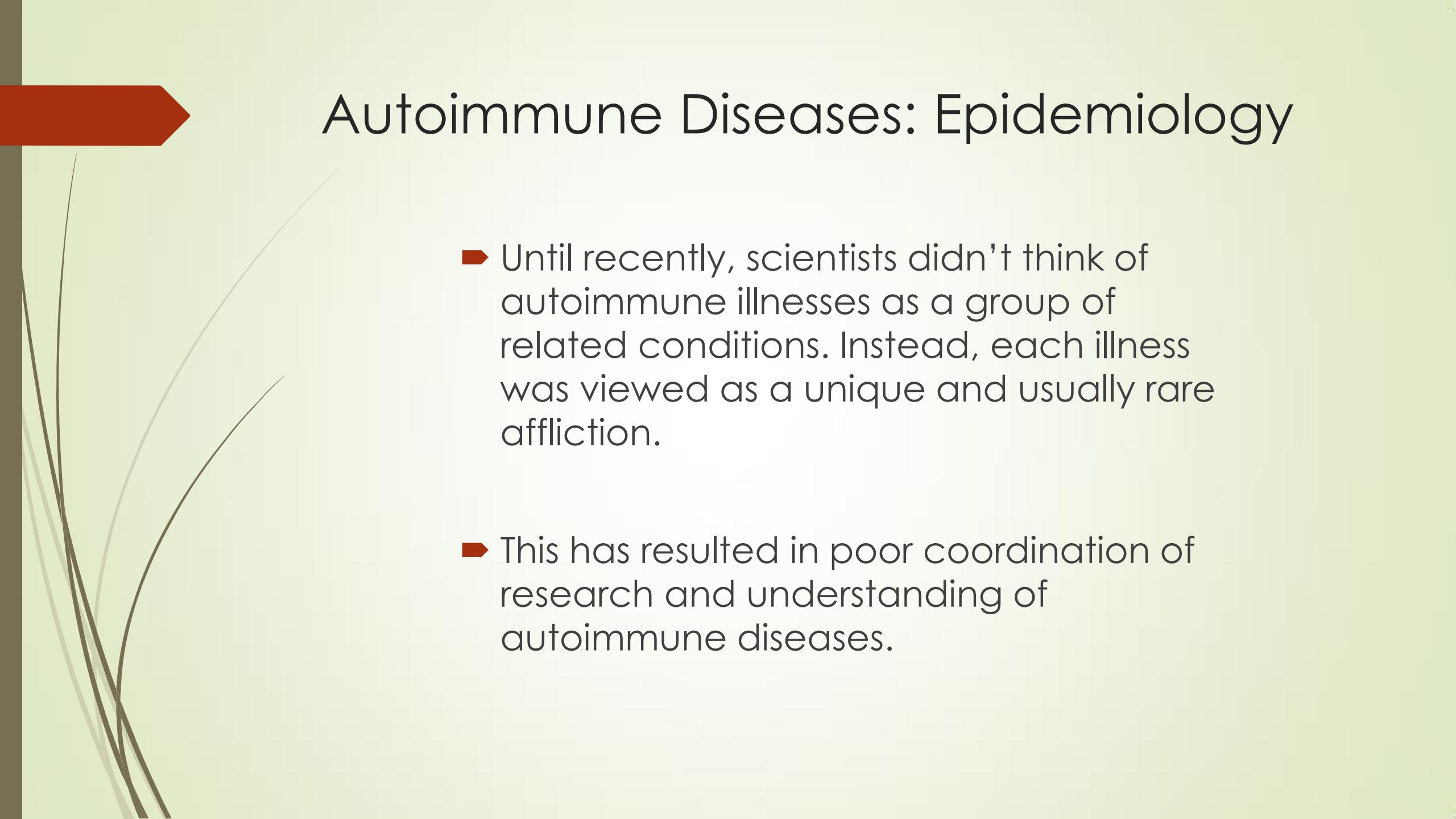
In an autoimmune reaction, antibodies and immune cells target the body's own healthy tissues by mistake, signaling the body to attack them.

Autoimmune Diseases

- ▶ alopecia areata
- ▶ autoimmune hemolytic anemia
- ▶ autoimmune hepatitis
- ▶ Dermatomyositis
- ▶ diabetes (type 1)
- ▶ some forms of juvenile idiopathic arthritis
- ▶ Glomerulonephritis
- ▶ Graves' disease
- ▶ Guillain-Barré syndrome
- ▶ pernicious anemia
- ▶ polyarteritis nodosa
- ▶ Polymyositis
- ▶ primary biliary cirrhosis
- ▶ Psoriasis
- ▶ rheumatoid arthritis
- ▶ scleroderma/systemic sclerosis
- ▶ Sjögren's syndrome
- ▶ systemic lupus erythematosus
- ▶ multiple sclerosis
- ▶ pemphigus/pemphigoid

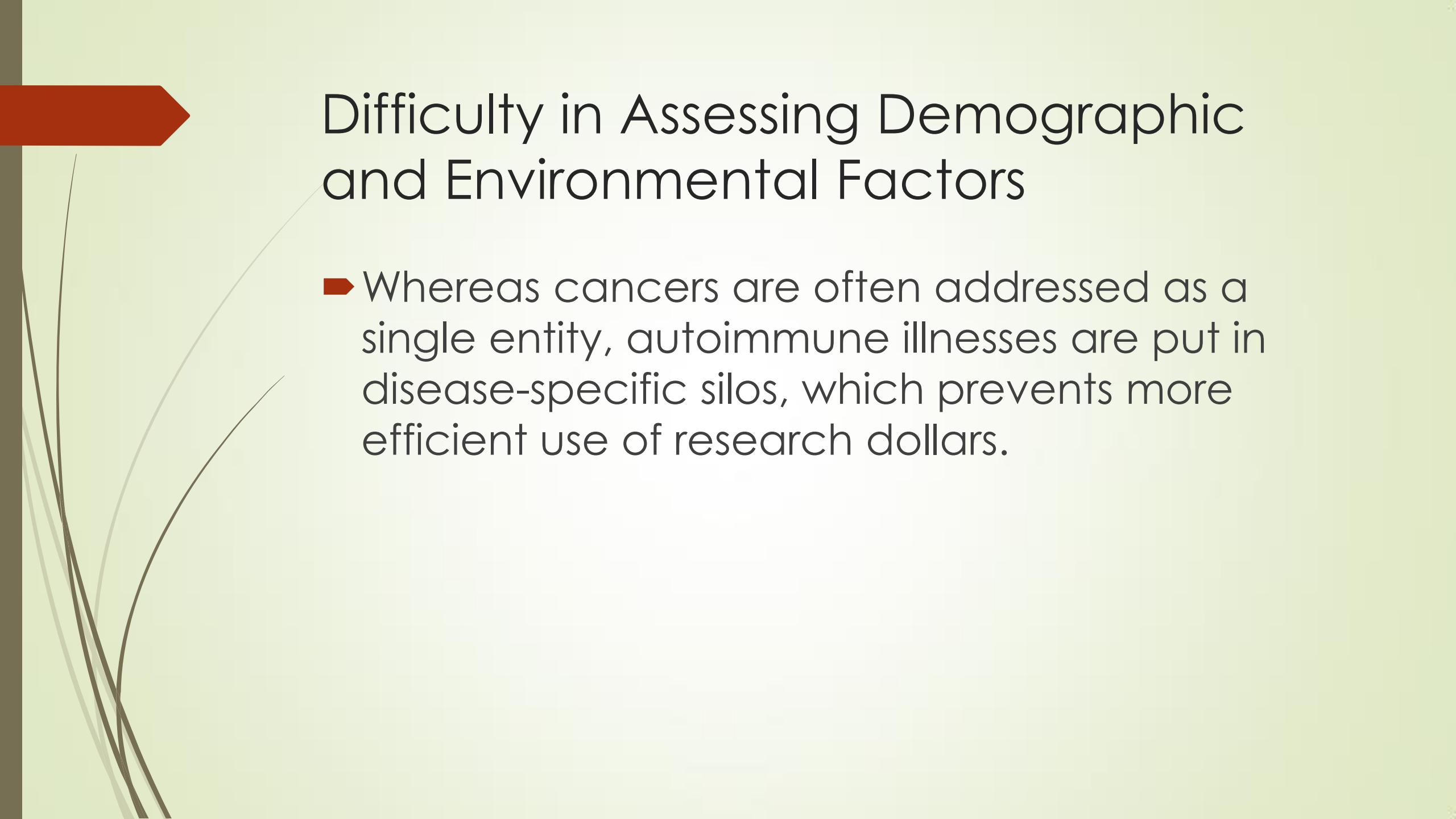
Autoimmune Diseases

- ▶ Behcet's syndrome
- ▶ Celiac disease
- ▶ Crohn's Disease
- ▶ Epidermolysis bullosa
acquisita
- ▶ Erythema nodosum
- ▶ Kawasaki disease
- ▶ idiopathic
thrombocytopenic
purpura
- ▶ myasthenia gravis
- ▶ Autism Spectrum
Disorder (suspected)
- ▶ some forms of thyroiditis
- ▶ some forms of uveitis
- ▶ some forms of
myocarditis
- ▶ vitiligo
- ▶ granulomatosis with
polyangiitis (Wegener's)



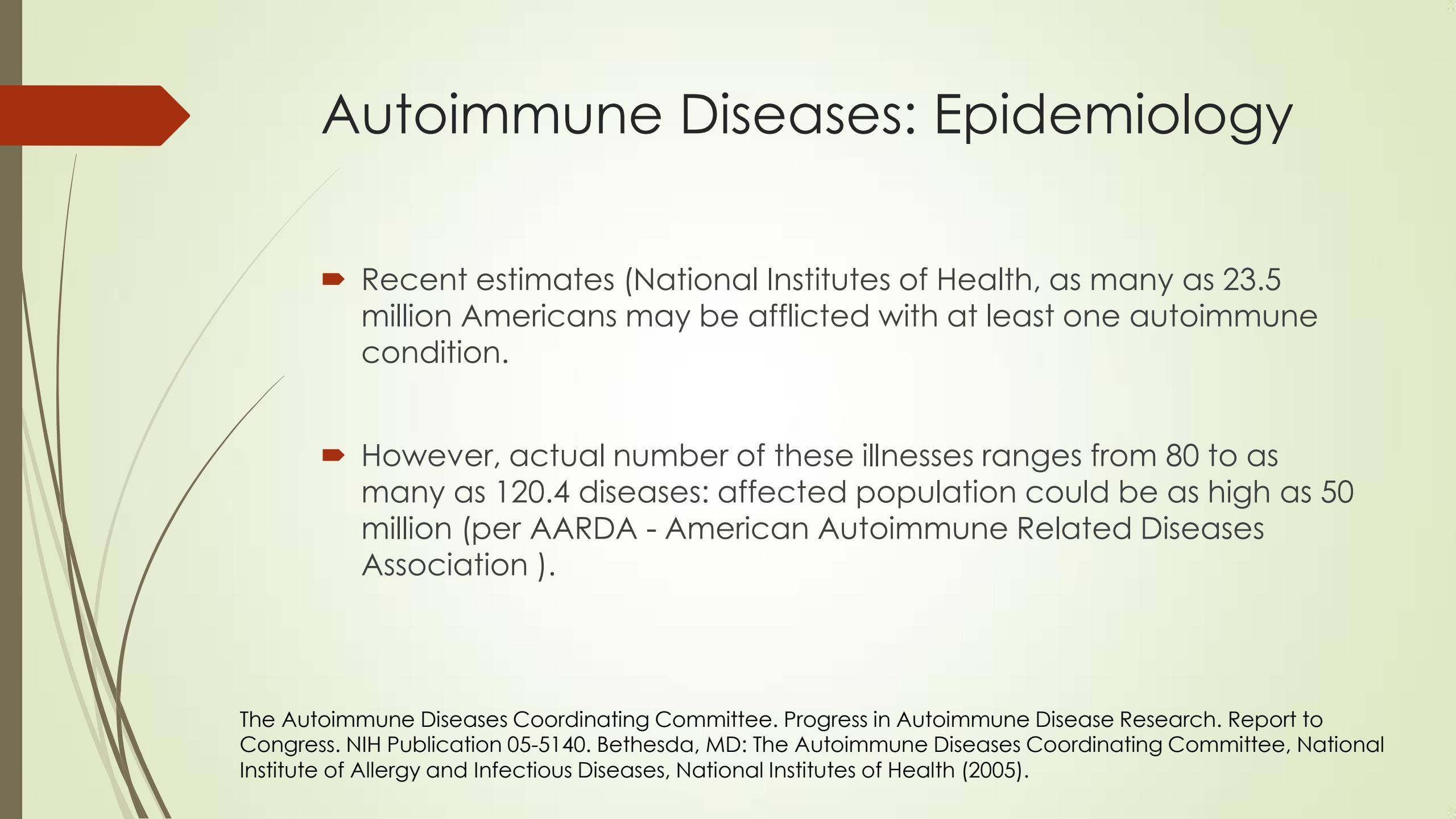
Autoimmune Diseases: Epidemiology

- ▶ Until recently, scientists didn't think of autoimmune illnesses as a group of related conditions. Instead, each illness was viewed as a unique and usually rare affliction.
- ▶ This has resulted in poor coordination of research and understanding of autoimmune diseases.



Difficulty in Assessing Demographic and Environmental Factors

- Whereas cancers are often addressed as a single entity, autoimmune illnesses are put in disease-specific silos, which prevents more efficient use of research dollars.



Autoimmune Diseases: Epidemiology

- ▶ Recent estimates (National Institutes of Health, as many as 23.5 million Americans may be afflicted with at least one autoimmune condition.
- ▶ However, actual number of these illnesses ranges from 80 to as many as 120.4 diseases: affected population could be as high as 50 million (per AARDA - American Autoimmune Related Diseases Association).

The Autoimmune Diseases Coordinating Committee. Progress in Autoimmune Disease Research. Report to Congress. NIH Publication 05-5140. Bethesda, MD: The Autoimmune Diseases Coordinating Committee, National Institute of Allergy and Infectious Diseases, National Institutes of Health (2005).

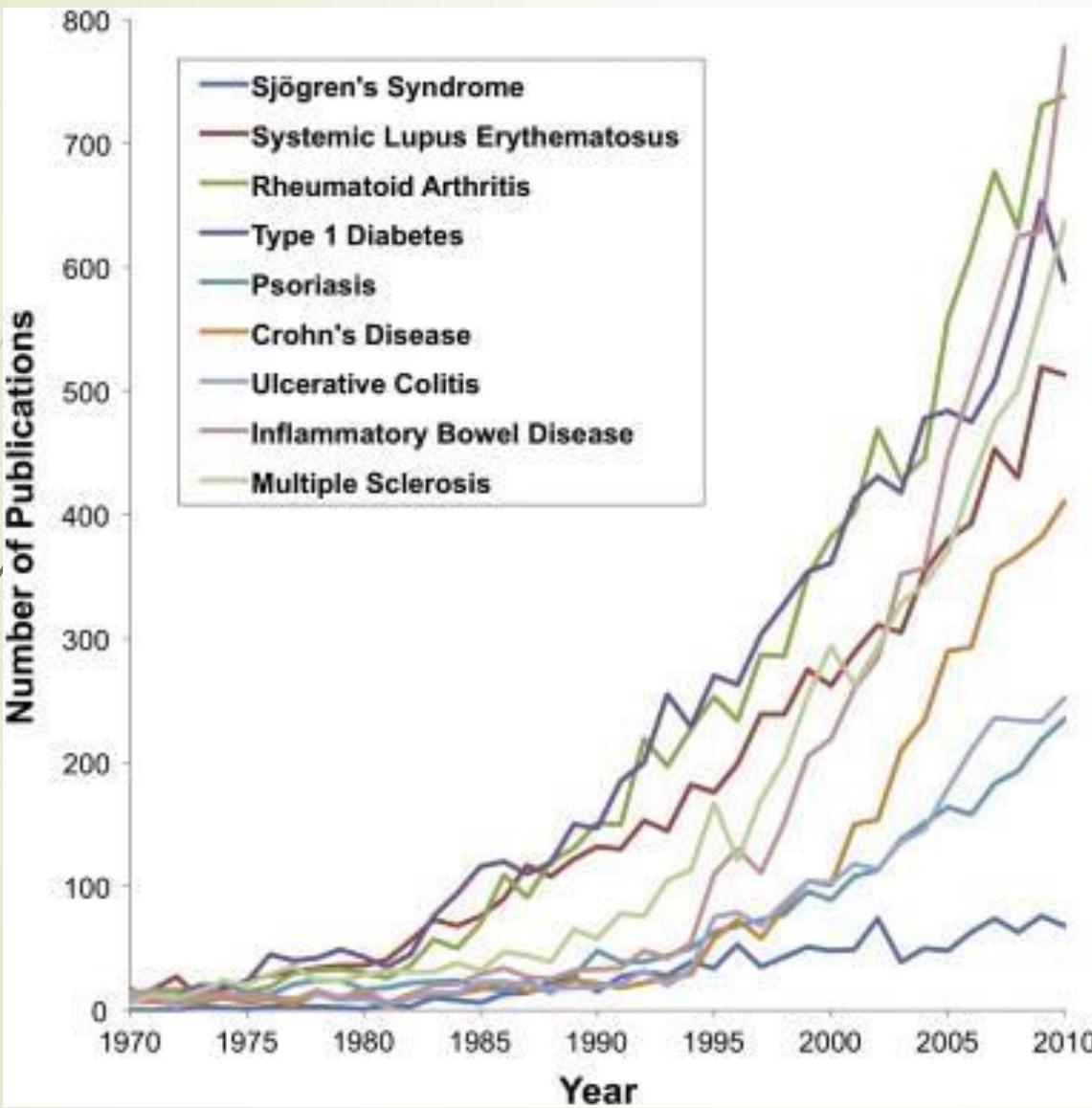
Autoimmune Disease: Statistics

- ▶ **Two third are women**
- ▶ **One of the top 10 leading causes of death in Female children and women up to the age of 64 years.**

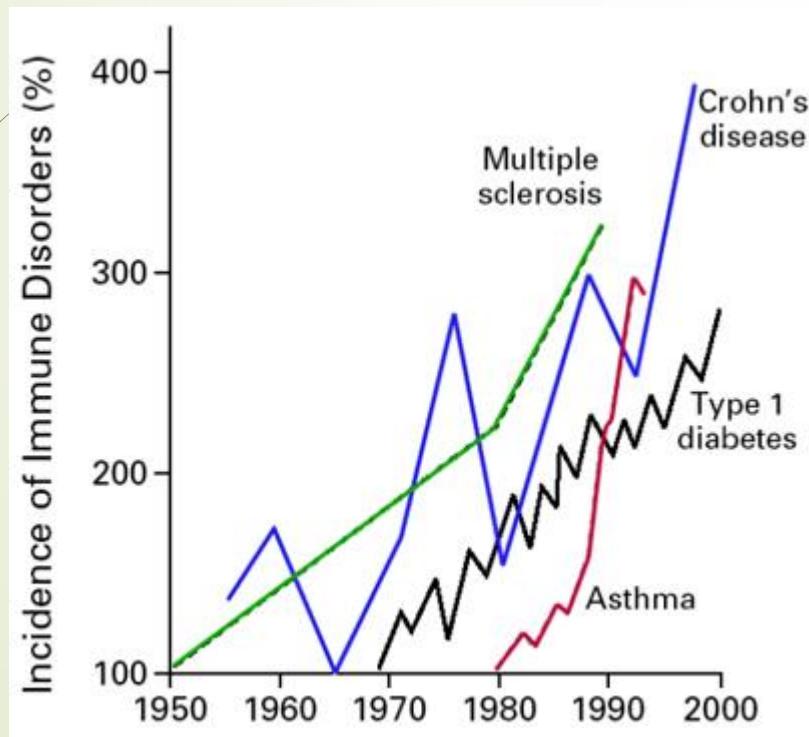
Direct Health care costs:

- ▶ **Autoimmune Disease: \$100 billion/year (NIH)**
 - ▶ **Funding \$591 million (2003 NIH)**
- ▶ **Cancer: \$57 billion/year (NIH, ACS)**
 - ▶ **Funding \$6.1 billion/year (2003 NIH)**
- ▶ **Heart disease \$200 billion/year (NIH, AHA)**
 - ▶ **Funding \$2.4 billion/year (2003 NIH)**

Rising Incidence of Autoimmune Diseases



Genetics of Sjögren's syndrome in the genome-wide association era
Journal of Autoimmunity, Volume 39, Issue 1, Pages 57-63
J A. Ice, H Li, et al.



From: Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med.* Sep 2002;347(12):911–920.

Immune Dysregulation

- ▶ Environmental Allergy/Sensitivities
- ▶ Food Sensitivities
- ▶ Eczema
- ▶ Asthma
- ▶ Autoimmune Diseases
- ▶ Ulcerative colitis
- ▶ Crohn's Disease
- ▶ Autism*
- ▶ PANDAS*
- ▶ Rheumatoid arthritis
- ▶ Alopecia



*What can we do
about it?*





Genetics and Epigenetics

- ▶ Genetic and environmental factors affect this progression (or lack of progression). Typically, **autoimmune antibodies begin to form in the body 3.5–7 years prior to the onset of symptoms; some individuals may manifest autoimmune antibodies on blood tests for decades without ever developing clinical illness.**
- ▶ Importantly is that environmental factors can influence this and is the basis for the biomedical/functional medicine approach along with Chinese medicine and Homeopathy.

When a patient is sick, the doctor should first regulate the patient's diet and lifestyle"

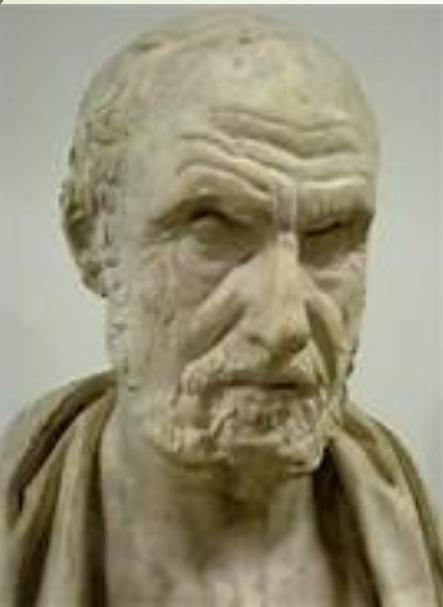
Sun Si-Miao



Nurture

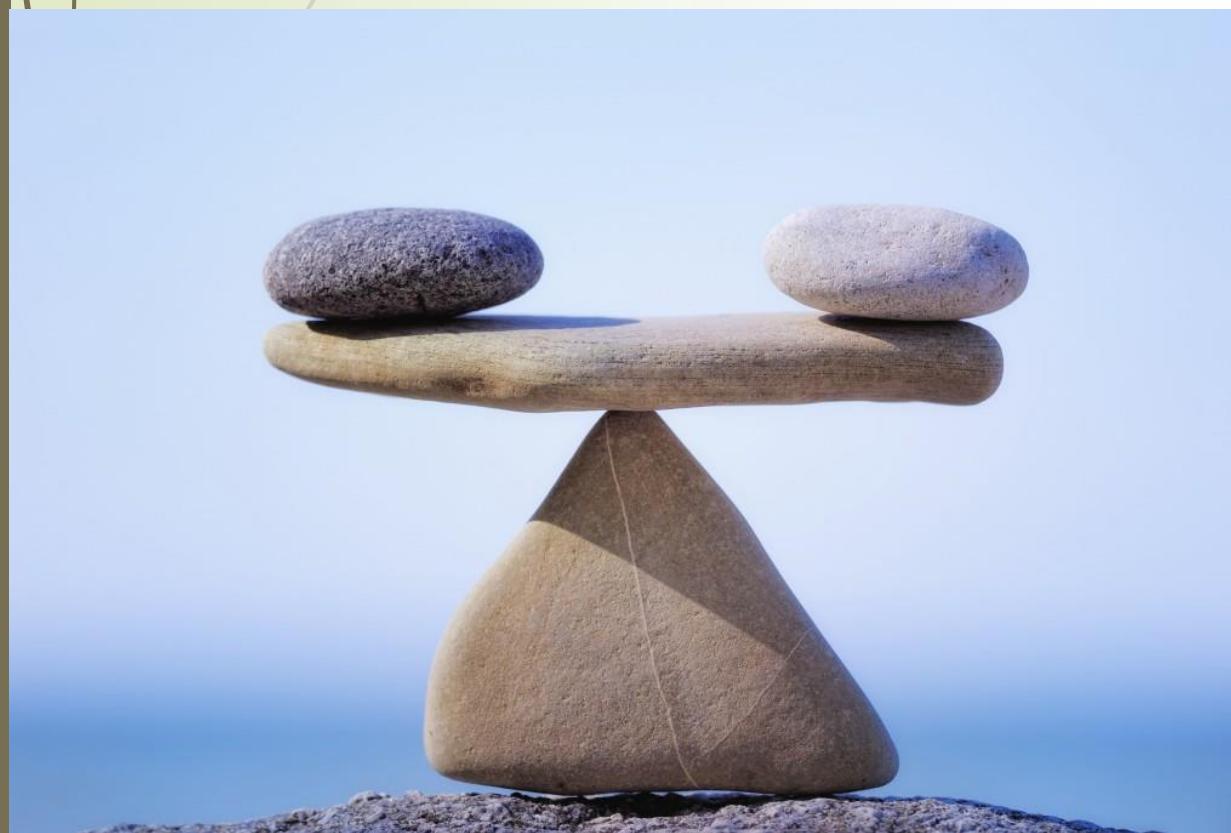
Illnesses do not come upon us from out of the blue. They are developed from small daily sins against nature. When enough sins have accumulated, illness will suddenly appear.

Hippocrates (400 B.C.)





It is all about Balance and Harmony





People don't need supplements, vitamins or minerals ...
but...

“Only if they eat wild, fresh, whole, organic, local, nongenetically modified food grown in virgin mineral and nutrient rich soils and not transported across vast distances and stored for months before being eaten. And if they work and live outside, breathe only fresh unpolluted air, drink only pure clean water, sleep 9 hours a night, move their bodies every day, and are free from chronic stressors and exposure to environmental toxins”

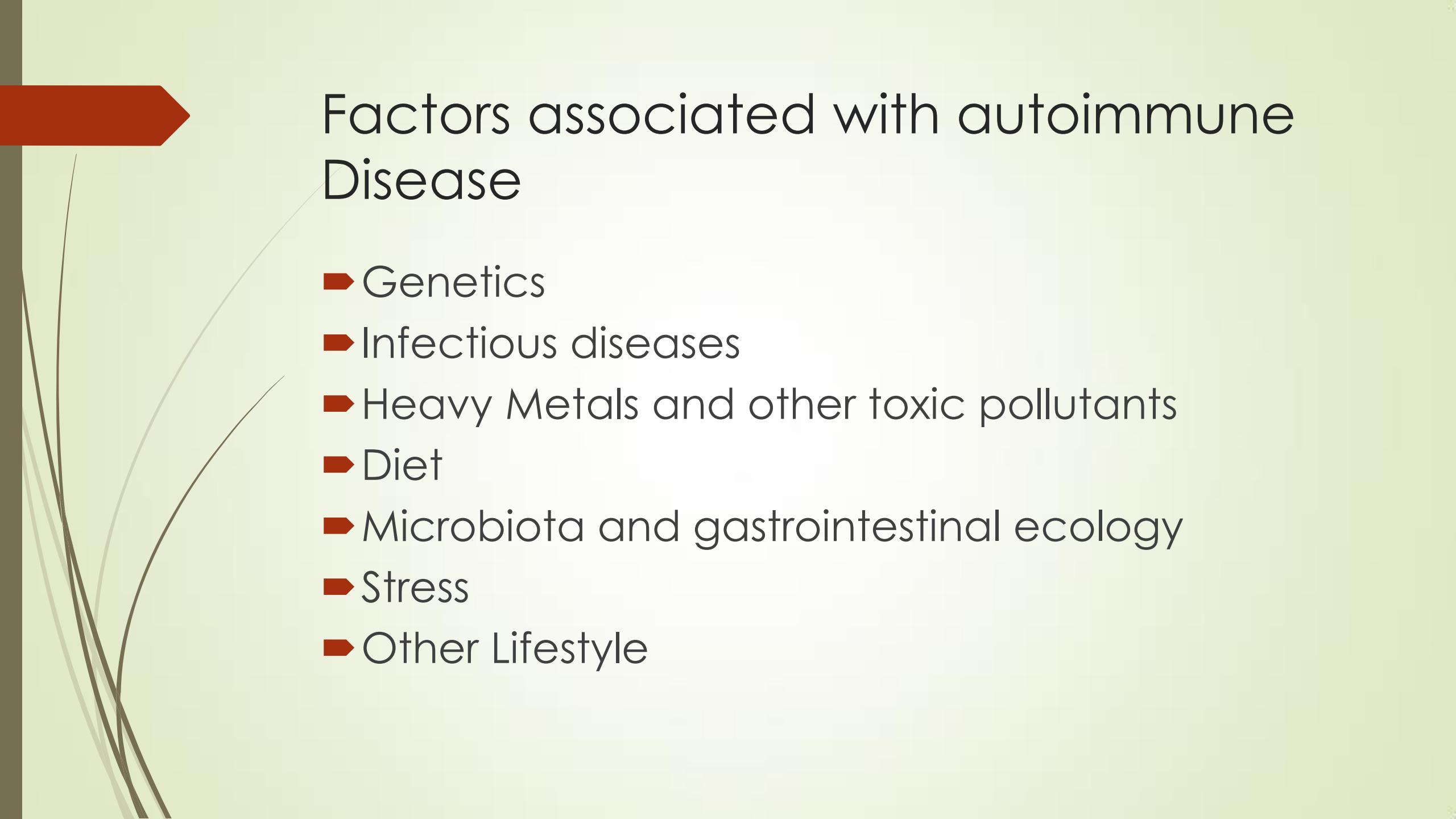
Mark Hyman: Institute for Functional Medicine



Environmental factors

Diet and lifestyle

Opportunity for new “targets”



Factors associated with autoimmune Disease

- ▶ Genetics
- ▶ Infectious diseases
- ▶ Heavy Metals and other toxic pollutants
- ▶ Diet
- ▶ Microbiota and gastrointestinal ecology
- ▶ Stress
- ▶ Other Lifestyle

Infections

- “In addition to genetic factors, environmental triggers (in particular viruses, bacteria and other infectious pathogens) are thought to play a major role in the development of autoimmune diseases.”*

*A. M. Ercolini and S. D. Miller. The role of infections in autoimmune disease. *Clinical and Experimental Immunology*, 155: 1–15



Marie-Antoinette

What she really said:

Qu'ils mangent de la terre
(Let them eat dirt)



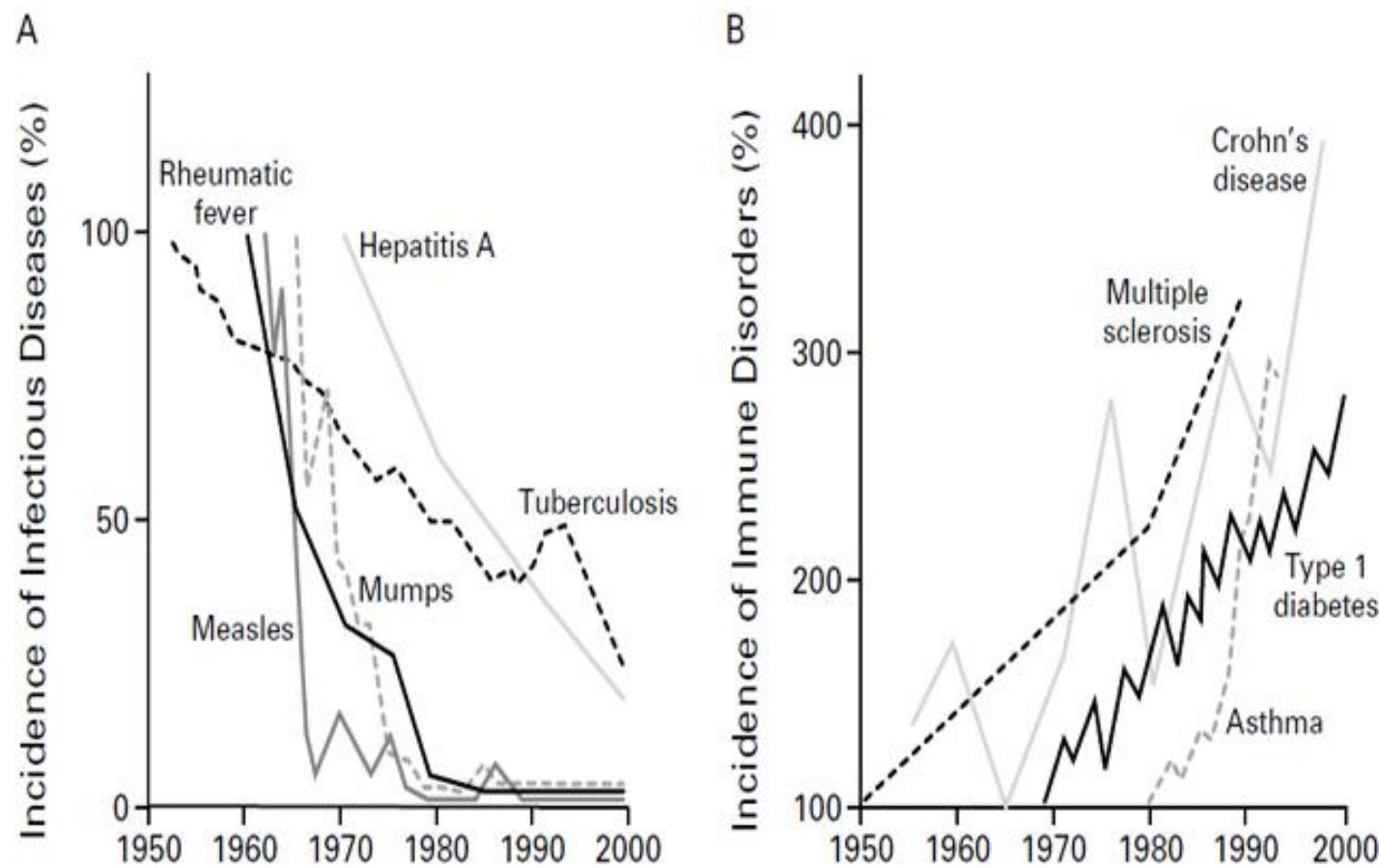


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussem et al.¹² In Panel B, data on immune disorders are derived from Swarbrick et al.,¹⁰ Dubois et al.,¹³ Tuomilehto et al.,¹⁴ and Pugliatti et al.¹⁵



Autoimmune Disease and the Environment

► Food Sensitivities

- Individuals with autoimmune disease have food sensitivities - There are many anecdotes of individuals who show marked improvement or resolution of symptoms of rheumatoid arthritis in conjunction with elimination of a particular food. There are also many individuals with autoimmune disease who feel better when consuming an anti-inflammatory diet, in conjunction with fish oil supplementation.

► Environmental toxins

- Numerous substances in our environment, including heavy metals, phthalates, BPA, xenoestrogens, and persistent organic pollutants might interfere with normal immune system function, and thus contribute to clinical manifestations of an autoimmune condition.

Toxins, pollutants and Heavy Metals

- “We’ve got 80,000 chemicals approved for use in commerce, but we know very little about their immune effects. Our lifestyles are also different than they were a few decades ago, and we’re eating more processed food. Should prevalence rates for heart disease and cancer continue their decline, Miller says, autoimmune diseases could become some of the costliest and most burdensome illnesses in the United States.”

Fred Miller, director, Environmental Autoimmunity Group at the National Institute of Environmental Health Sciences in: volume 119 | number 6 | June 2011 • Environmental Health Perspectives **Environmental Factors in Autoimmune Disease**
Charles W. Schmidt, MS



There is an association between Autoimmune Disease and environmental Toxicants

- ▶ Hemdan NY, Emmrich F, Faber S, Lehmann J, Sack U. **Alterations of TH1/TH2 reactivity by heavy metals: possible consequences include induction of autoimmune diseases.** Ann N Y Acad Sci. 2007 Aug;1109:129-37.
- ▶ Mishra KP. **Lead exposure and its impact on immune system: a review.** Toxicol In Vitro. 2009 Sep;23(6):969-72.
- ▶ Bahadar H, Abdollahi M, Maqbool F, Baeeri M, Niaz K. **Mechanistic overview of immune modulatory effects of environmental toxicants.** Inflamm Allergy Drug Targets. 2015;13(6):382-6.
- ▶ Suzuki Y, Inoue T, Ra C. **Autoimmunity-inducing metals (Hg, Au and Ag) modulate mast cell signaling, function and survival.** Curr Pharm Des. 2011 Nov;17(34):3805-14.

Autoimmune Disease and the Environment

- ▶ Sources of air pollution including traffic and probably solid fuels are associated with Rheumatoid Arthritis
- ▶ ACPA (the most specific biological markers with predictive and prognostic value in Rheumatoid Arthritis patients) are elevated in patients' sera five to 10 years prior to diagnosis with RA, suggesting that factors initiating autoimmunity in RA may act before appearance of symptoms and signs characteristic of clinical disease.

Is air pollution a risk factor for rheumatoid arthritis?

Mickael Essouma and Jean Jacques N. Noubiap. Journal of Inflammation (2015) 12:48



SICK BUILDING SYNDROME

VOCs are a large group of carbon based toxins that are invisible and often have no odour. They are found in a number of everyday household products and furnishings including synthetic carpets and cannot be eradicated by traditional cleaning methods. VOCs are responsible for sick building syndrome and have a number of negative effects on our health, causing skin allergies including eczema, respiratory problems and even cancer.

XYLENE

Nose/throat irritation
Loss of co-ordination
Liver damage

METHYLENE CHLORIDE

Memory loss
Headaches
Damage to nervous system

TOLUENE

Dry cracked skin
Nausea
Nervous system damage

ACETONE

Dizziness
Respiratory tract irritation
Eye irritation

FORMALDEHYDE

Burning sensation in eyes/skin
Nausea
Cancer

ETHYLENE GLYCOL

Depression
Vomiting
Respiratory failure

BENZENE

Headaches
Rapid/irregular heartbeat
Unconsciousness

PERCHLOROETHYLENE

Mood/behavioural changes
Eye/throat irritation
Drowsiness



Diet





“When diet is wrong, medicine is of no use; When diet is correct, medicine is of no need.”

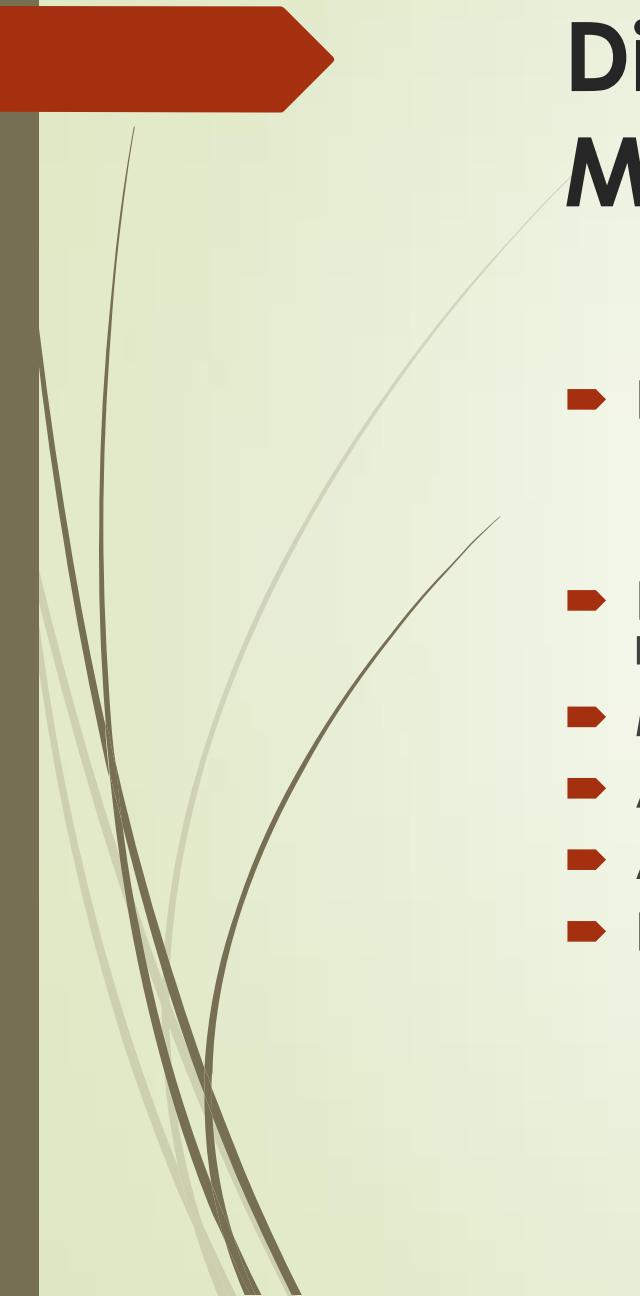
Ayurvedic Proverb

“Dietary therapy should be the first step when one treats a disease. Only when this is unsuccessful should one try medicine.”

Sun Sí-Míao

“death sits in the bowels” and “bad digestion is the root of all evil”.

Hippocrates (400 B.C.)



Diet in Children (from a Chinese Medicine Perspective)

- ▶ Keep foods simple
 - ▶ Rice or oats
 - ▶ Carrots and related foods (strengthen “spleen”)
- ▶ Foods should be well cooked (not overly cooked and not too many raw foods)
- ▶ Minimize strong flavors
- ▶ Avoid flours for the first two years (mucus producing)
- ▶ Avoid added sugars and starches and artificial sweeteners
- ▶ Pleasant and unhurried relationship with food and eating
 - ▶ Eat slowly, relax with a calm mind



Balance in Life: Eating (from a Chinese Medicine Perspective)

- Nourish the core: Stomach/Spleen
 - Grains: Oats, rice, millet, corn
 - Vegetables: Carrots, cabbage, fennel, potatoes, peas, squash, soy beans
 - Fruits: Apples, dates, figs, grapes, papaya
 - Most meats and fish (particularly cold water)
 - Warming Apertifs (for adults) before or after meals

**“Knowing how to treat the center is knowing
how to bring all networks into balance”**
Ming Dynasty (AD 1368-1644)

Fruits and Vegetables

- ▶ Ancestors ate over 500 varieties of vegetables over lifetime
- ▶ Contain over 25,000 phytonutrients
- ▶ Vegetables to day have less nutritious content (soil/environment/variety)
- ▶ What to eat:
 - ▶ Preferably minimal amount of starchy vegetables. Deeper shades of greens and colors are the best (even starchy vegetables like potatoes)
 - ▶ Look for Heirloom varieties
 - ▶ Corn is not a vegetable (and may contain as much as 44% sugar (sweet corn))

Eating on the Wild Side by Jo Robinson

Getting Kids to eat vegetables:

Deceptively Delicious: Simple Secrets to Get Your Kids Eating Good Food by Jessica Seinfeld (2008)

The Sneaky Chef: Simple Strategies for Hiding Healthy Foods in Kids' Favorite Meals by Missy Chase Lapine (2007)

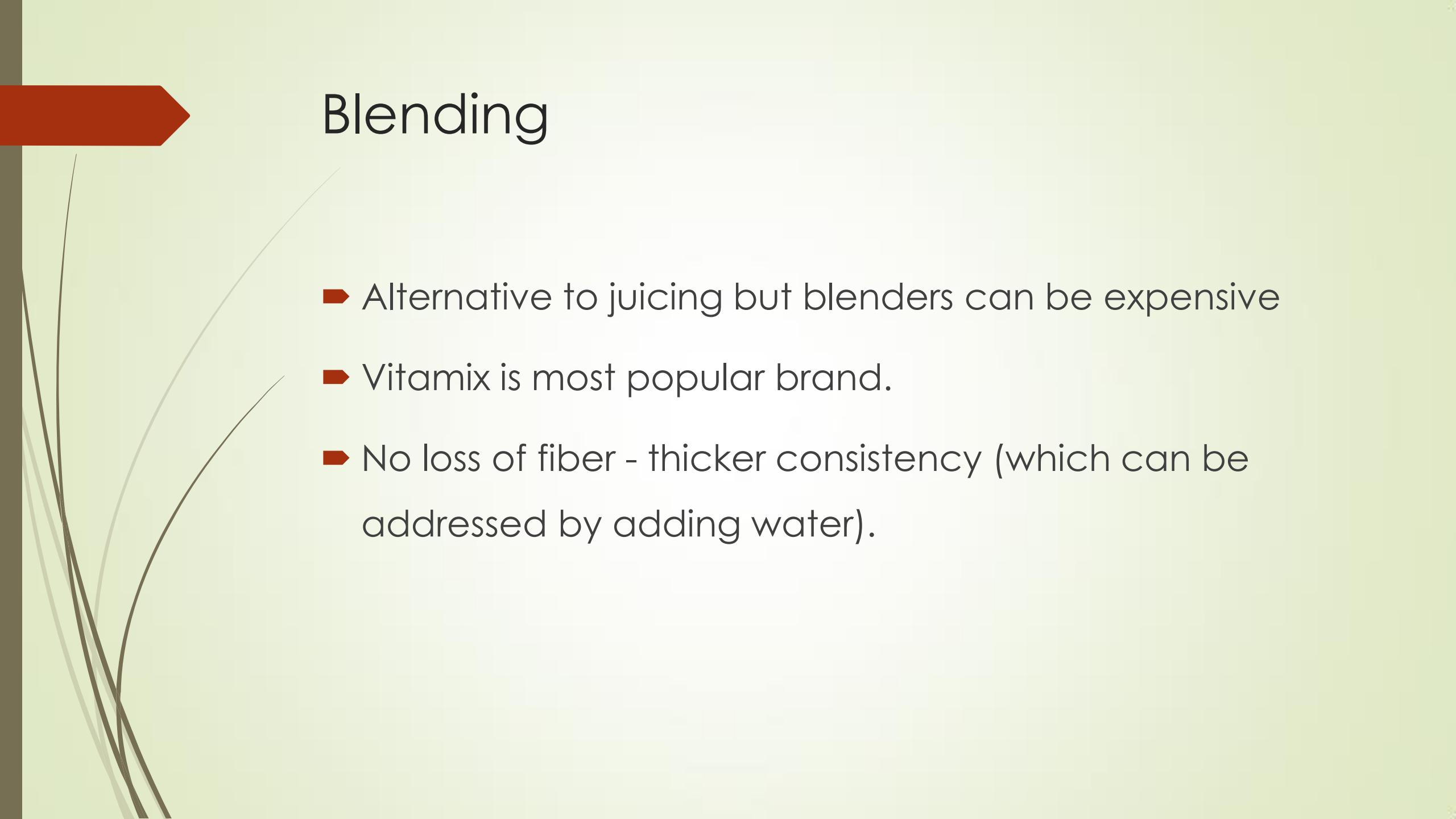


Juicing and Blending

- ▶ Especially for children who don't eat fruits/vegetables.
- ▶ Vegetables to use: include cabbage, spinach, carrots, broccoli, parsley, and oregano, mixed with a small amount of fresh fruit for flavor and other nutrients.
- ▶ May start with higher quantity of fruit and slowly increase the vegetable to fruit ratio.
- ▶ Organic vegetables and fruits are preferred (less toxics/pesticides).
- ▶ Target about 8 ounces/day should be enough for most children and adults, adjust for size and age of children.

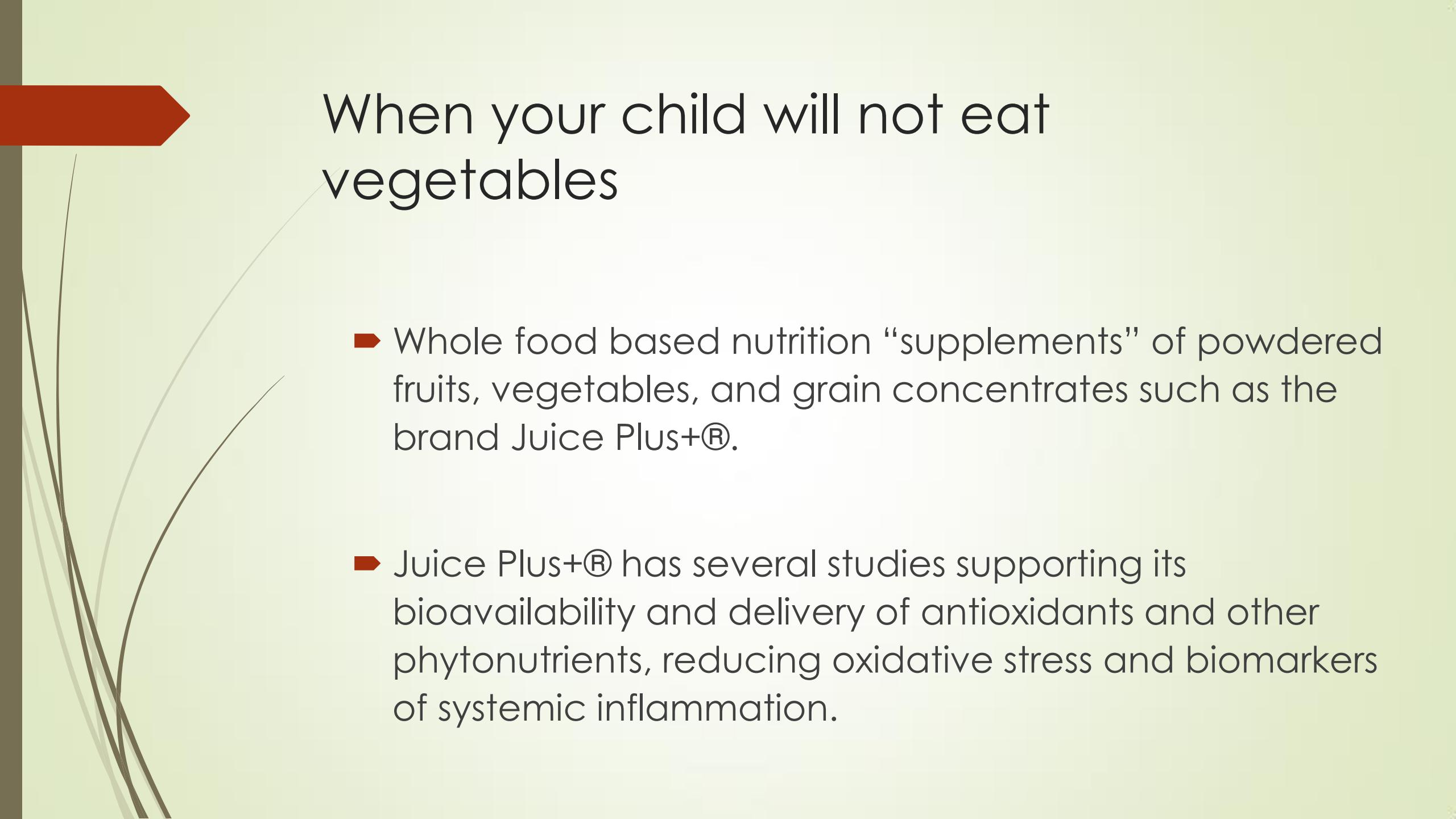
Juicing

- ▶ Requires juicer: fresh vegetable/fruit juice
- ▶ Take fresh or store for up to a few days in an airtight glass container.
- ▶ Provides the missing vitamins, minerals, and 25,000 recognized other phyto nutrients.
- ▶ Commercial juices are “pasteurized” causes a loss of some nutrients, especially vitamins.
- ▶ Strains out the pulp. Grinding one time provides only about half of the original vitamins/minerals, so after the first juicing it is useful to soak the pulp for about 15 minutes in a small amount of pure water (about 10% of the amount of liquid initially squeezed out), and then grind the pulp again – recover most of the remaining vitamins/minerals.
- ▶ Disadvantage to juicing is a loss of insoluble fiber (the soluble fiber remains) both are beneficial.



Blending

- ▶ Alternative to juicing but blenders can be expensive
- ▶ Vitamix is most popular brand.
- ▶ No loss of fiber - thicker consistency (which can be addressed by adding water).



When your child will not eat vegetables

- ▶ Whole food based nutrition “supplements” of powdered fruits, vegetables, and grain concentrates such as the brand Juice Plus+®.
- ▶ Juice Plus+® has several studies supporting its bioavailability and delivery of antioxidants and other phytonutrients, reducing oxidative stress and biomarkers of systemic inflammation.

Oils and Fats

- ▶ pathway interactions of fatty acid (FA) conversion to eicosenoids is complex the primary core issue is the competition of both omega-6 and omega-3 FAs for the delta-6 desaturase (D6D) enzyme that determines whether the end product is pro- or anti-inflammatory. In general, the greater amount of LA in the diet the more AAs are created (pro-inflammatory) and the less ALA is converted to EPA (anti-inflammatory).
- ▶ Ancestral diet: omega 6 to omega 3 ratio of 1:1 or 2:1.
- ▶ Current western diet the omega 6 to omega 3 ratio estimated to range from 10–20–30:1. Change occurred with the advent of food processing

Dietary Oils

- ▶ Choose oils (and products made with): **cold-pressed, expeller-pressed, or naturally pressed oils.**
 - ▶ Olive oils
 - ▶ Nut oils
 - ▶ Avocado oils
 - ▶ Coconut oils
 - ▶ Butter (yes, butter – from grass fed cows)
- ▶ **Eliminate**
 - ▶ Many prepared/processed foods contain vegetable, corn, peanut, or soybean oil. Often extracted with hexane (commonly used as a cleaning agent and solvent)
 - ▶ **Blended Vegetable Oils:** Most commercial vegetable oils are a mixture of unidentified oils that have been extracted with chemicals.
 - ▶ **Old Oils:** Oils have limited shelf life, no more than a year. Oils should smell fresh.
 - ▶ **Oils High in Polyunsaturates:** Include corn oil and soybean oil, among others.
 - ▶ **Vegetable Shortenings:** Usually made with partially hydrogenated oils.
 - ▶ **Partially hydrogenated oil:** source of trans fats

A close-up, high-magnification image showing a dense, layered community of microorganisms. The top layer consists of numerous blue, oval-shaped bacteria, likely lactobacilli, arranged in a tight, overlapping pattern. Below this, a layer of red, textured material, possibly a substrate or another type of microorganism, provides a contrasting background. The overall appearance is one of a healthy, diverse microbial ecosystem.

Colonic Flora

(We're not alone)



Food For Thought



Pro/Prebiotics: Maintenance of a Healthy GI tract: History

Paleolithic ancestors

- ▶ Billions more lactic acid bacteria
- ▶ Increased fiber intake
 - ▶ Many more times vegetables
 - ▶ 500 different plant species

Pro/Prebiotics: A Normal Part of Your “Daily Bread” ?



- ▶ **Earlier human diet included:**
 - ▶ fermented foods containing bacteria (used for food preservation)
 - ▶ More fiber and fermentable foods
- ▶ **Advent of processed foods:**
 - ▶ lack of fermented foods and fiber
 - ▶ Increase in allergies, inflammatory conditions, cancers, etc.

Pro/Prebiotics: A Normal Part of Your “Daily Bread” ?



- ▶ Benefits of fermented foods:
 - ▶ Increased shelf life
 - ▶ Increased nutrient bioavailability (Breakdown of protein and release of Ca and Mg)
 - ▶ Vitamin production

Summary on Probiotics and Prebiotics

- ▶ **Probiotics and Prebiotics are a good thing**
 - ▶ Convincing evidence for their use in:
 - ▶ Acute (viral) diarrhea
 - ▶ Antibiotic associated diarrhea
 - ▶ C. difficile infections
 - ▶ May be therapeutic for:
 - ▶ Allergies, atopic dermatitis
 - ▶ Inflammatory Bowel disease
 - ▶ NEC, colic
 - ▶ Prevention of cancers
 - ▶ Good safety record
 - ▶ Complex area requiring much more research
 - ▶ Should be a part of everyone's diet

Stress



Stress and Autoimmunity

- “Psychological stress, recognized as a public health issue in children and young adults, may be one mechanism to induce and maintain autoimmunity in children... A number of them (studies on stress and autoimmunity) have observed that the autoimmune disease itself causes psychological stress.”
- Childhood traumatic stress increased the likelihood of hospitalization with a diagnosed autoimmune disease decades into adulthood. These findings are consistent with recent biological studies on the impact of early life stress on subsequent inflammatory responses.

Faresjö M. The Link between Psychological Stress and Autoimmune Response in Children. Crit Rev Immunol. 2015;35(2):117-34.

Dube SR, Fairweather D, Pearson WS, Felitti VJ, Anda RF, Croft JB. Cumulative childhood stress and autoimmune diseases in adults. *Psychosom Med.* 2009 Feb;71(2):243-50.

Stress and Autoimmunity

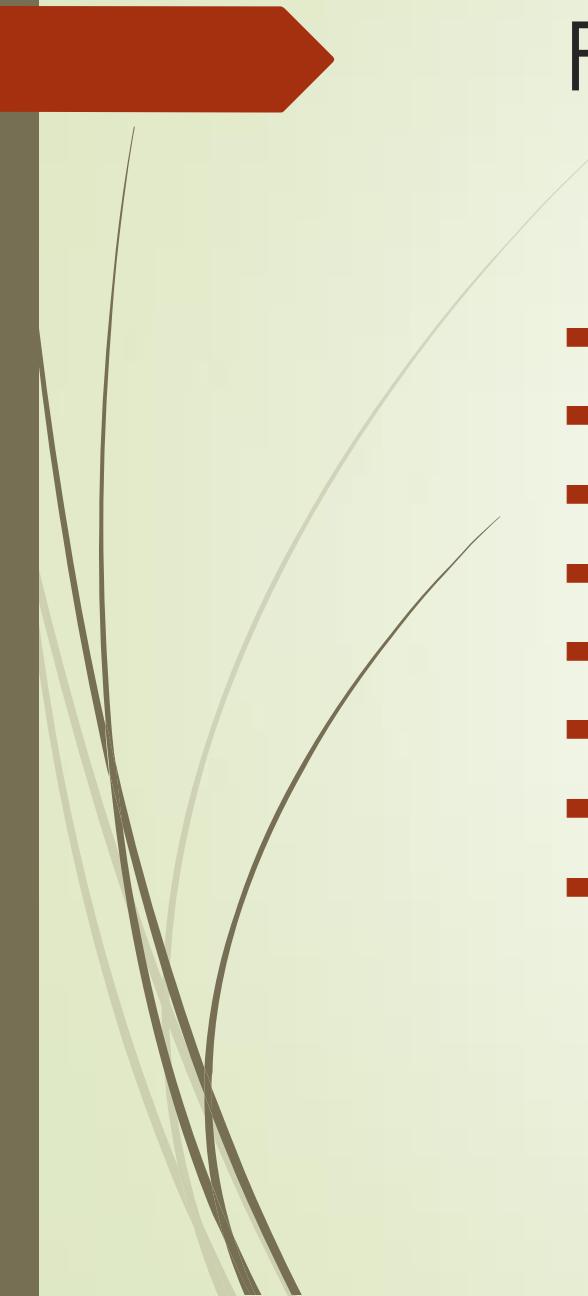
- ▶ Ten retrospective case-control studies were found. Nine studies showed a positive association between stress and development/onset of T1D in children, adolescents or adults. One study did not find an association between stress and development/onset of T1D.
- ▶ Psychological stress, measured as psychosocial strain in the family, seems to be involved in the induction, or progression, of diabetes-related autoimmunity in the child during the 1st year of life.

Sepa A¹, Ludvigsson J. Psychological stress and the risk of diabetes-related autoimmunity: a review article. *Neuroimmunomodulation.* 2006;13(5-6):301-8.

Sepa A, Wahlberg J, Vaarala O, Frodi A, Ludvigsson J. Psychological stress may induce diabetes-related autoimmunity in infancy. *Diabetes Care.* 2005 Feb;28(2):290-5.

Summary





Factors associated with Health

- ▶ Determine and eliminate “sensitive” foods (often Dairy and Gluten)
- ▶ Nurture the gastrointestinal Ecosystem
- ▶ Organic, nutrient rich anti-inflammatory and microbiome supportive diet
- ▶ Avoidance of Pollutants and toxicants
- ▶ Adequate restful Sleep
- ▶ Adequate Physical activity
- ▶ Adequate periods of rest and relaxation
- ▶ Maintain emotional and mental balance
 - ▶ Emotionally and mentally supportive environment
 - ▶ Counter stress and stressful events



Books and Sources

- ▶ Deep Nutrition: Why Your Genes Need Traditional Food (2017) by Catherine Shanahan M.D
- ▶ Food Rules: An Eater's Manual 2009 by Michael Pollan
- ▶ Eating on the Wild Side (2013) by Jo Robinson
- ▶ Deceptively Delicious: Simple Secrets to Get Your Kids Eating Good Food (2008) by Jessica Seinfeld
- ▶ The Sneaky Chef: Simple Strategies for Hiding Healthy Foods in Kids' Favorite Meals (2007) by Missy Chase Lapine

Panacea for health

In the past, people practiced the Tao... They understood the principle of balance, of Yin and Yang... They ate a balanced diet at regular times, arose and retired at regular hours, avoided overstressing their bodies and minds, and refrained from overindulgences of all kinds. They maintained well-being of body and mind; thus, it is not surprising that they lived over one hundred years.



From the Neijing Suwen: The Yellow Emperor's Classic of internal medicine,
translation by Maoshing Ni