



Environmental Influence in Autoimmune Diseases

Mark Gourley, MD



THE MYOSITIS ASSOCIATION



[News Home](#) - [Yahoo!](#) - [Help](#)

[News](#) [Finance](#) [Sports](#) [Entertainment](#)

Welcome, Guest

[Personalize News Home Page](#) - [Sign In](#)

Yahoo! News Wed, Apr 30, 2003 Search for Search [Advanced](#)

[News Front Page](#) > [Full Coverage](#) > [Health](#)

Study: Traffic Pollution May Damage Sperm Quality, Male Fertility

Opinion & Editorials

- [Testing mothers for HIV](#) - Chicago Tribune (registration req'd) (Apr 28, 2003)
- [WalkAmerica: Help increase the odds for the most fragile of babies](#) - Detroit Free Press (Apr 25, 2003)
- [Simply saving babies](#) - Indianapolis Star (Apr 24, 2003)
- [A reproduction law of lengthy gestation](#) - Globe and Mail. (Apr 18, 2003)

[more](#)

Yahoo! Categories

- [Infertility](#)
- [Pregnancy and Birth](#)
- [Reproductive Health](#)

Latest Developments

[Traffic Pollution May Damage Sperm Quality](#)

(Reuters) - Traffic pollution may affect male fertility by damaging sperm, Italian scientists said on Wednesday. After studying 85 attendants at tollgates on Italian motorways, researchers at the University of Naples in southern Italy discovered the men had poorer-quality sperm than other young and middle-aged Italian workers in the same area. "The sperm count did not differ significantly between our study group and the controls, but in general the sperm of the study group was more feeble and less active, so it has a lower fertility potential," said Dr. Michele de Rosa, a researcher at the university.

[More ...](#)

- [Traffic pollutants affect fertility in men](#) - abstract (Human Reproduction)
- [Shanghai pollution hits male fertility](#) - Nov 2000 (BBC)
- [Environmental causes of infertility](#) (USF) | [Message board](#)

News Stories

- [Pollution can affect male fertility: study](#) - Australian Broadcasting Corporation (Apr 30, 2003)
- [Traffic pollution damages men's sperm](#) - New Scientist (Apr 30, 2003)
- [Traffic 'damages male fertility'](#) - BBC (Apr 30, 2003)
- [Car Exhaust Chokes Sperm](#) - HealthScout (Apr 30, 2003)
- [Traffic Pollution May Damage Sperm Quality](#) - Reuters (Apr 30, 2003)



[News Home](#) - [Yahoo!](#) - [Help](#)

[News](#) [Finance](#) [Sports](#) [Entertainment](#)

Welcome, Guest

[Personalize News Home Page](#) - [Sign In](#)

Yahoo! News Thu, Apr 17, 2003 Search for Search [Advanced](#)

[News Front Page](#) > [Full Coverage](#) > [World](#)

Study: Small Amounts of Lead Can Cause Neurological Damage in Children

Yahoo! Categories

- [Pollution](#)
- [more](#)

Feature Articles

- [From EPA Plan, a Whiff of Danger](#) - Washington Post (Apr 15, 2003)
- [Level of lead not high near smelter](#) - Detroit Free Press (Apr 10, 2003)
- [Car commuters prefer luxury of guilt](#) - Sydney Morning Herald (Apr 8, 2003)
- [more](#)

Opinion & Editorials

- [One Huge Step for Cleaner Air](#) - NY Times (registration req'd) (Apr 16, 2003)
- [Minorities bear brunt of air pollution woes](#) - Columbia State (Apr 9, 2003)

Latest Developments

[Low Levels of Lead Damage Children](#)

(HealthScout) -- Two studies offer more worrisome news about the harm done to children by lead exposure. One study says IQs are lowered significantly by levels of lead in the blood below those now regarded as acceptable by U.S. health officials. The other finds delayed puberty in girls with elevated levels of the metal in their blood. The first study, of 172 children in the Rochester, N. Y., area, found lower IQs in those with blood lead levels of 10 micrograms per deciliter, which the U.S. Centers for Disease Control and Prevention (CDC) lists as acceptable. [More...](#)

- [Study abstract](#) (NEJM) | [Lead's Toxic Toll](#) (Detroit Free Press)
- Yahoo! Health: [Lead Poisoning](#) | [Message board](#)

News Stories

- [Even lower levels of lead can hurt kids](#) - Rochester Democrat & Chronicle (Apr 17, 2003)
- [Lead levels believed safe found harmful](#) - Baltimore Sun. (Apr 17, 2003)
- [Child lead-poisoning warning for Sydney](#) - Sydney Morning Herald (Apr 17, 2003)
- [Ontario power plant tied to pollution jump](#) - Toronto Star (Apr 17, 2003)
- [Canadian polluters worse than in U.S., report says](#) - Globe and Mail. (Apr 17, 2003)
- [Forecast clouded by ozone alert](#) - The Sun (Apr 17, 2003)

Toxic Shock: What We've Got in Our Bodies

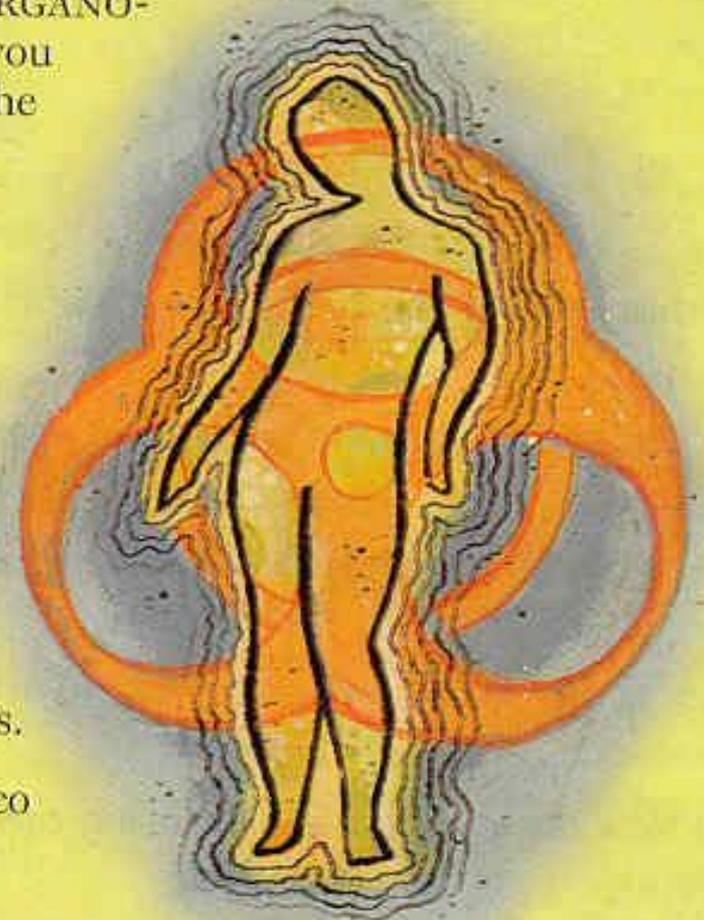
YOU MAY NEVER HAVE HEARD OF PHTHALATES OR ORGANO-phosphates, but according to a CDC report last week, you probably carry both types of chemicals in your body. The agency measured 27 chemicals in Americans. The findings:

LEAD: Levels of this heavy metal continue to drop in kids—encouraging, since it causes learning and behavioral problems. But children in some cities are still at high risk.

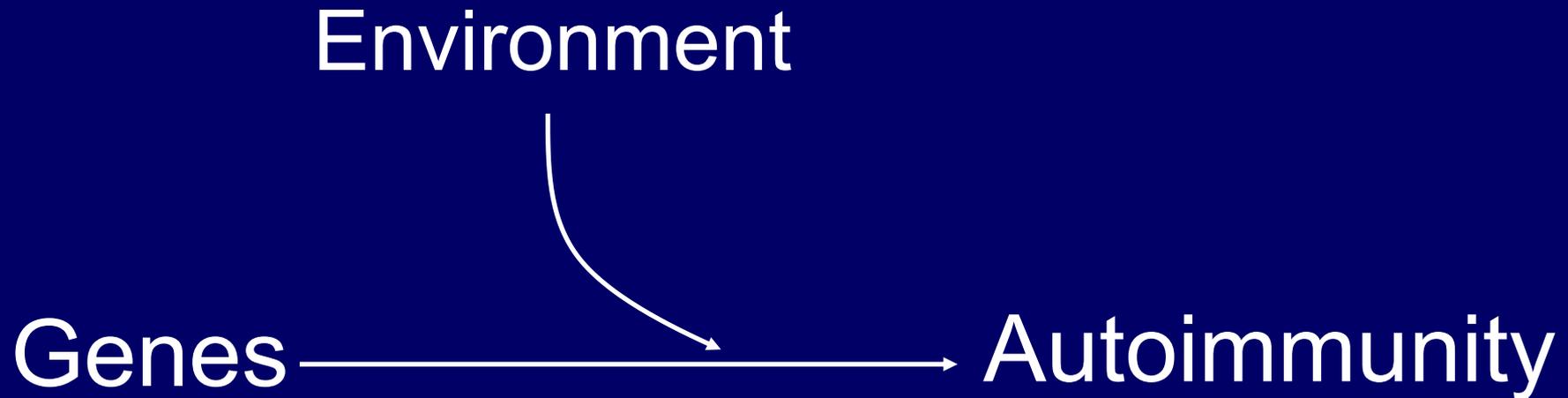
DIMETHYLPHOSPHATE: One of six pesticide byproducts measured, it was detected in most Americans. Some of DMP's parent pesticides cause cancer in animals, but researchers aren't sure how DMP itself affects humans.

MONO-BENZYL PHTHALATE: MBzP causes birth defects in animals. A byproduct of a chemical used in cosmetics, MBzP was found in most people—but it's not proven to harm humans.

COTININE: Cotinine levels—which indicate exposure to tobacco smoke—have dipped since the late '80s, offering proof that no-smoking regulations have public-health benefits.



Current Knowledge of Environment and Myositis



What Is an Environmental Exposure?

- Defined - susceptibility factors for an illness that are not inherited
- Two types:
 - Macroenvironment (uncontrolled)
 - Atmospheric pollution
 - Water contamination
 - Microenvironment (controlled)
 - Workplace
 - Diet
 - Leisure time

Immune-mediated Disease (IMD)

Autoimmunity

- Hundreds of acquired disorders in which the immune system likely play a pathogenic role
- Third most common group of diseases in the U.S.
 - After cardiac disease and cancer - and are becoming more common
- High rate of chronic illness and death resulting in great costs to society
- Pathogeneses are poorly understood but likely involve chronic immune activation after environmental exposures in genetically susceptible individuals

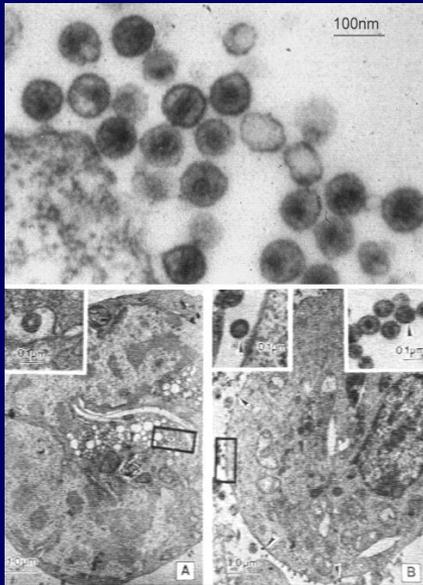
Types of Immune-mediated Disease

- Hypersensitivity and allergic disorders (allergic rhinitis, sinusitis, asthma)
- Adverse reactions to drugs, biologics, medical devices, foods (drug-induced lupus, vasculitis)
- Immune suppression and decreased ability to resist disease (polychlorinated biphenyls & respiratory infections)
- Organ-specific autoimmune diseases (Hashimoto's thyroiditis, type 1 diabetes)
- Systemic autoimmune diseases (myositis, rheumatoid arthritis, lupus, systemic sclerosis)

Possible Environmental Triggers of Immune-mediated Diseases

- Infectious agents
 - Bacteria / parasites: Streptococci, Borrelia, others
 - Viruses: +RNA, DNA, retroviruses, others
- Non-infectious agents
 - Foods: L-tryptophan, adulterated rapeseed oil
 - Drugs: D-penicillamine, hydralazine, many others
 - Biologics: Vaccines, cytokines
 - Medical devices: Collagen and silicone implants
 - Occupational exposures: Silica, beryllium, vinyl chloride
 - Other exposures: UV light, mercury, petrochemicals

Examples - Caprine Arthritis Encephalitis



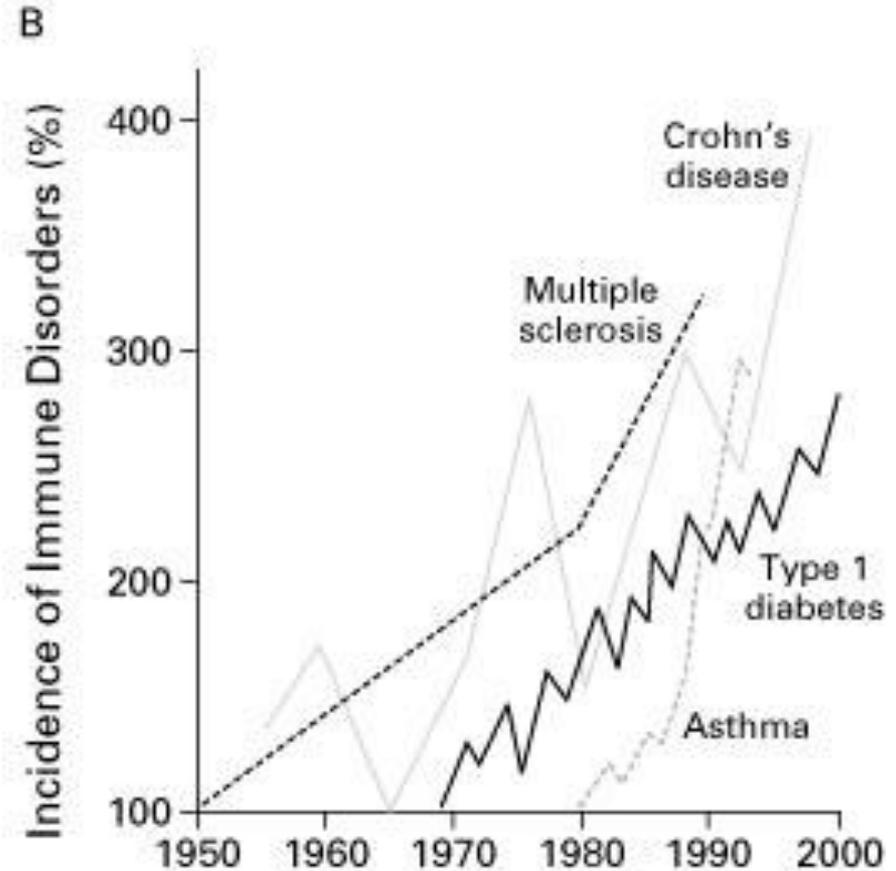
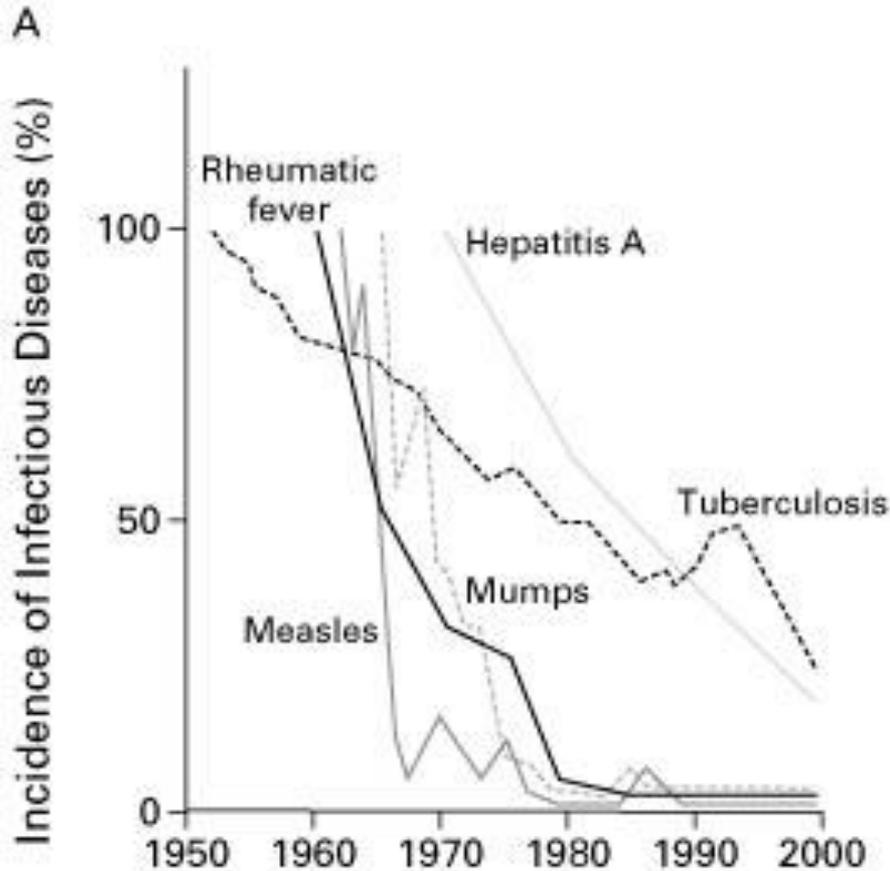
Caused by a virus

Erythema Infectiosum (Fifth Disease)



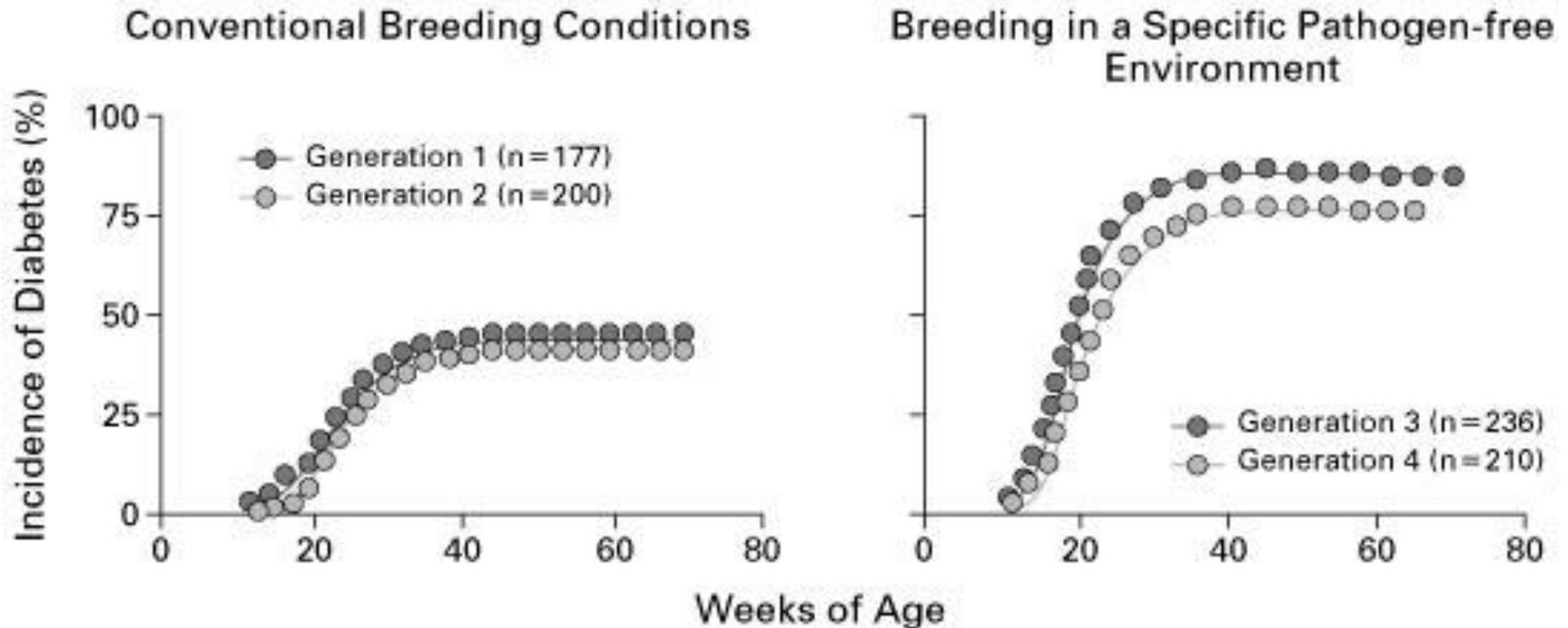
Caused by a virus

Infectious Disease and Autoimmunity



Some infections are decreasing while autoimmune disease is increasing.

Certain strains of mice develop diabetes when raised in specific germ free environments



Bacteria and viruses can be helpful for the immune system

Xenobiotics

- Chemicals found in the environment, drugs or in food that are not produced by the human body.
- Xenobiotics are capable of influencing the immune system.
- The number of xenobiotics that are capable of causing autoantibody formation is growing.

Animal Models of Autoimmunity Triggered by Xenobiotics

Xenobiotic	Animal Strain	Autoimmunity	Human counterpart
Mercury	Rats	Ab disease	Lupus
Gold	Rats	IC-kidney disease	Kidney inflammation
Penicillamine	Mice	Ab to a receptor	Myasthenia Gravis
Procainamide	Mice	ANA, lung disease	Lupus

Chemicals Associated With Autoimmunity

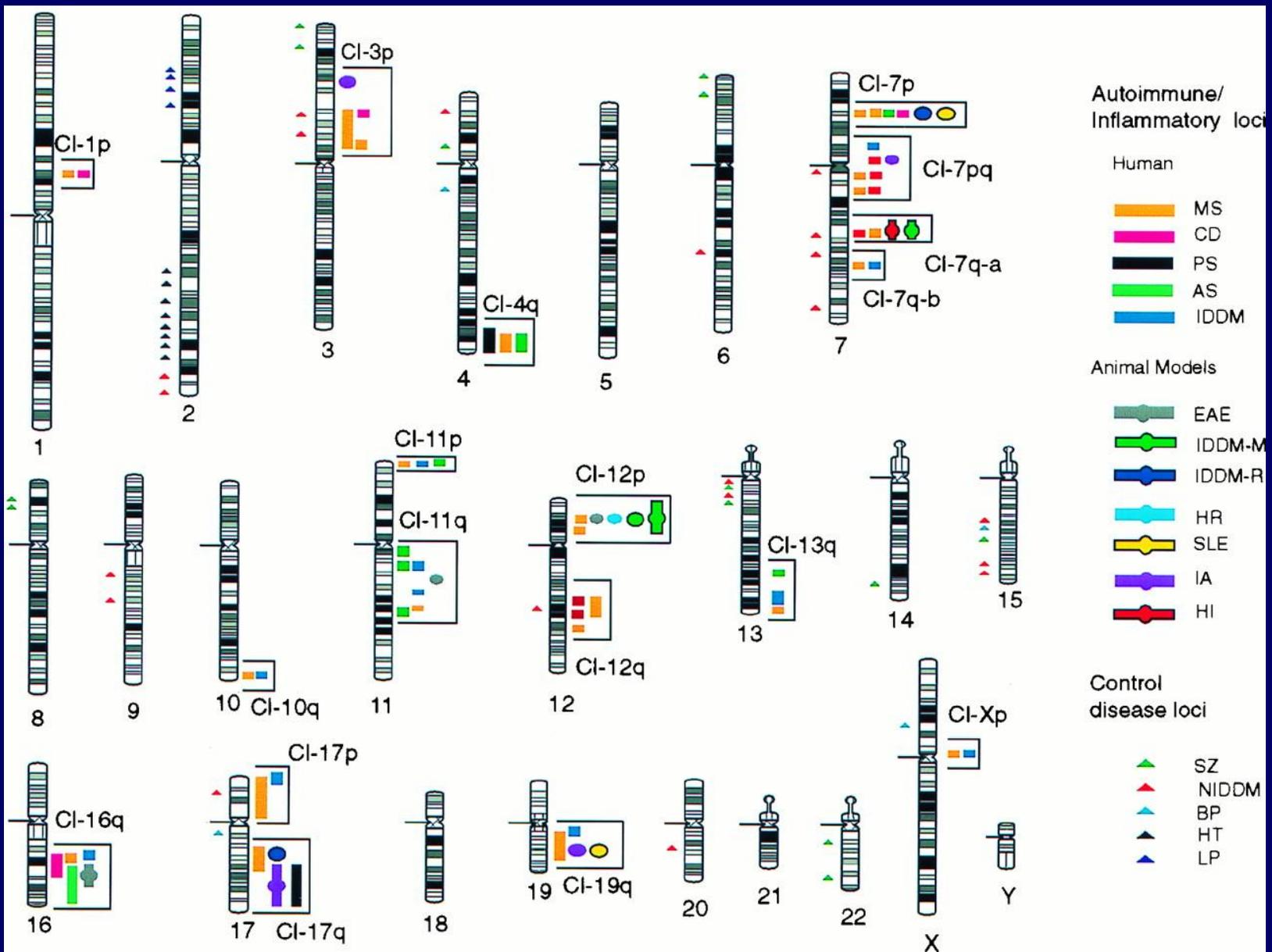
- SLE
 - Allopurinol, Carbamazepine, Cocaine, Dapsone, Gold, Hydralazine, INH, Penicillamine, Procainamide, Sulfonamides
- Scleroderma
 - Bleomycin, Silicon, Trilene, Vinyl chloride
- Cytopenias
 - Methyldopa, Gold, Penicillamine, Penicillin
- Renal disease
 - Cadmium, Gold, Mercury
- No good associations for myositis

Mechanisms Leading to Impaired Immunologic Tolerance

- Abnormal cytokine secretion
- Modified self antigen
- Abnormal MHC molecule expression
- Failure to delete autoreactive lymphocytes
- Lack of tolerance to autoreactive lymphs
- Abnormal adhesion molecule expression
- Antigen mimicry

Many different ways disease may occur

Genes are very important



Evidence for the Environment's Influence

- Less than 50% of identical twins get the disease
- Strong timing connection with some environmental exposures and disease onset
- Dechallenge = disease improvement after agent removal
- Rechallenge = disease recurrence after re-exposure
- Evidence from animal models
- Epidemiology studies between exposures and diseases

Myositis

- Group of syndromes whose hallmarks are chronic muscle weakness from muscle inflammation of unknown cause
- About 0.01% of US population affected; more common in women, frequent onset age 30s and 40s
- Dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) are the most common clinical forms
- Common problems include: muscle weakness, swelling of the hands and feet, pain and stiffness of the joints; rashes; GI (reflux, dysphagia and constipation); lung (ILD, fibrosis) involvement; Non-specific symptoms such as extreme fatigue, generalized weakness, weight loss, and vague aching of muscles, joints and bones

Global UV Light Levels Predict the Proportion of DM Around the World

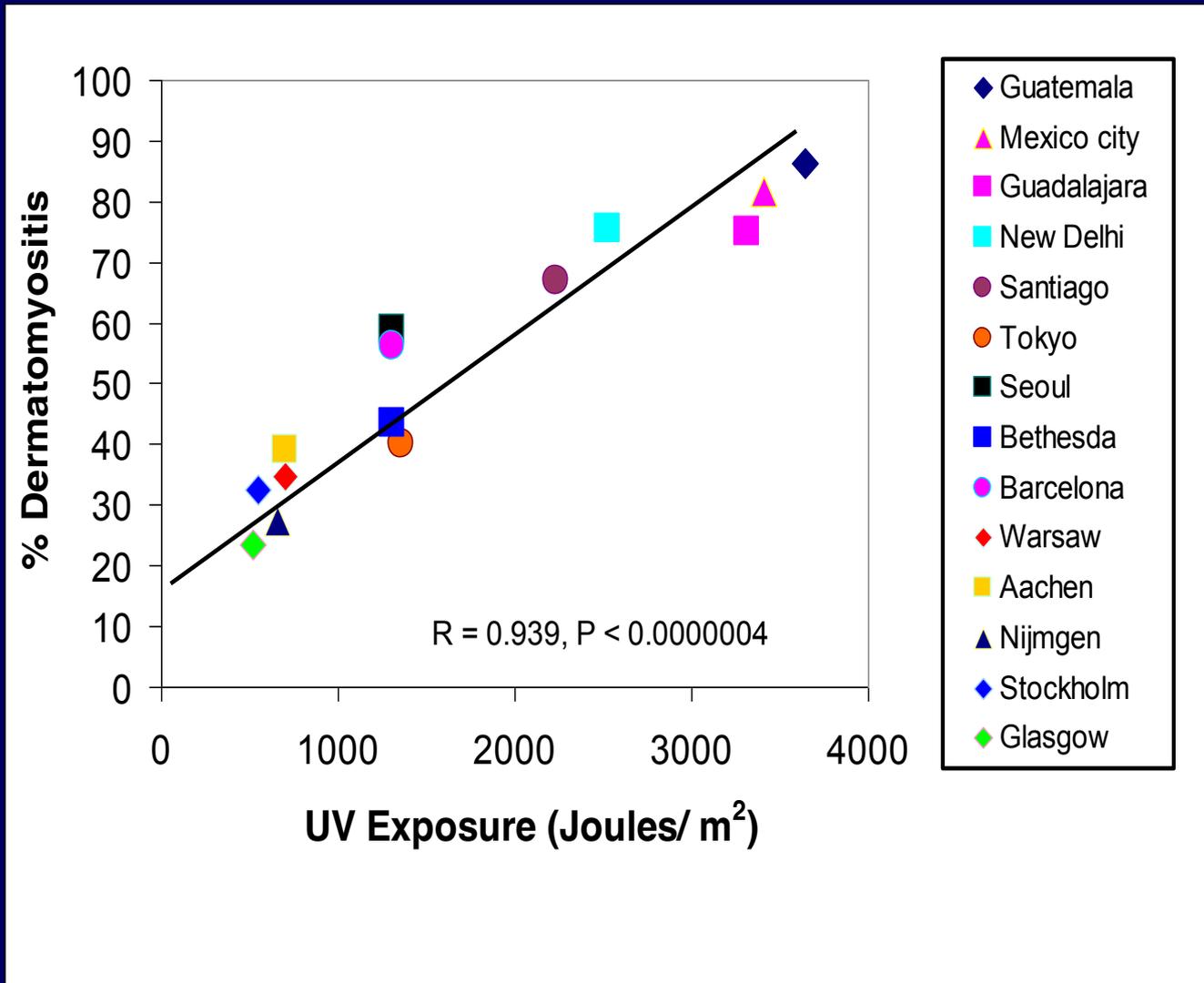
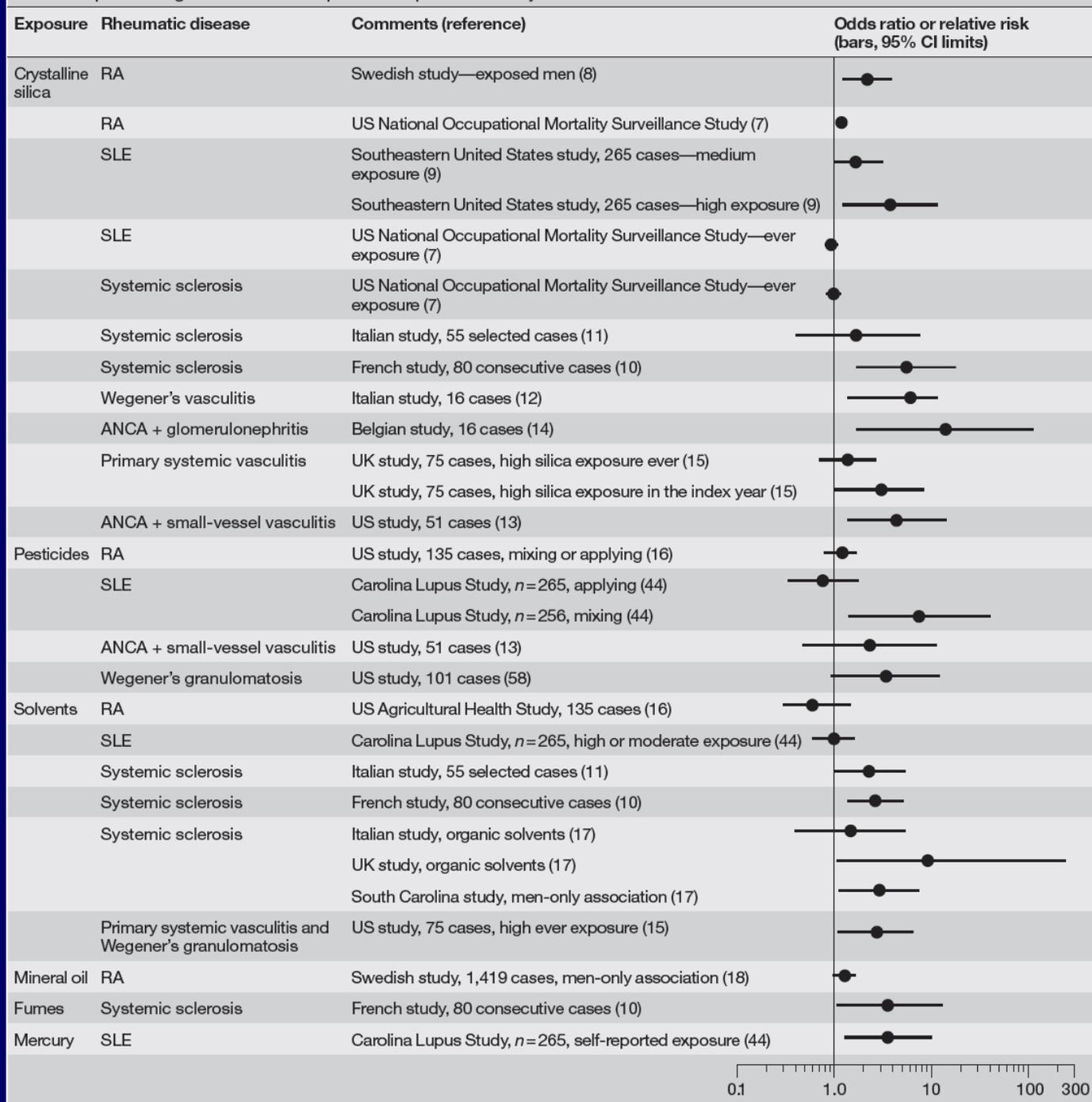
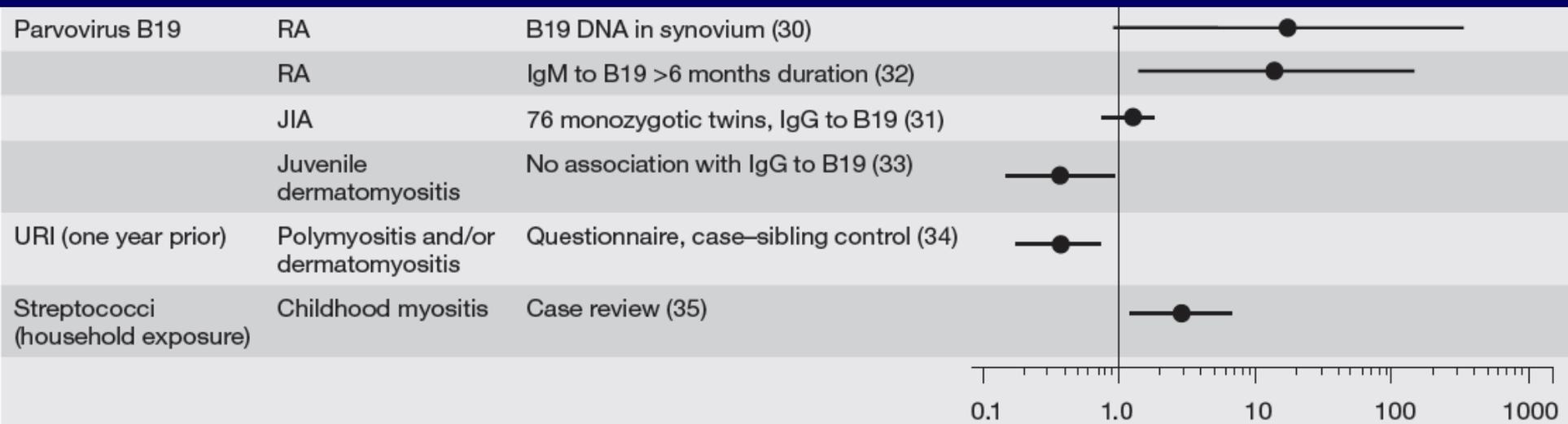


Table 1 Epidemiologic studies of occupational exposures and systemic rheumatic diseases.

Very Few Studies have looked at Myositis



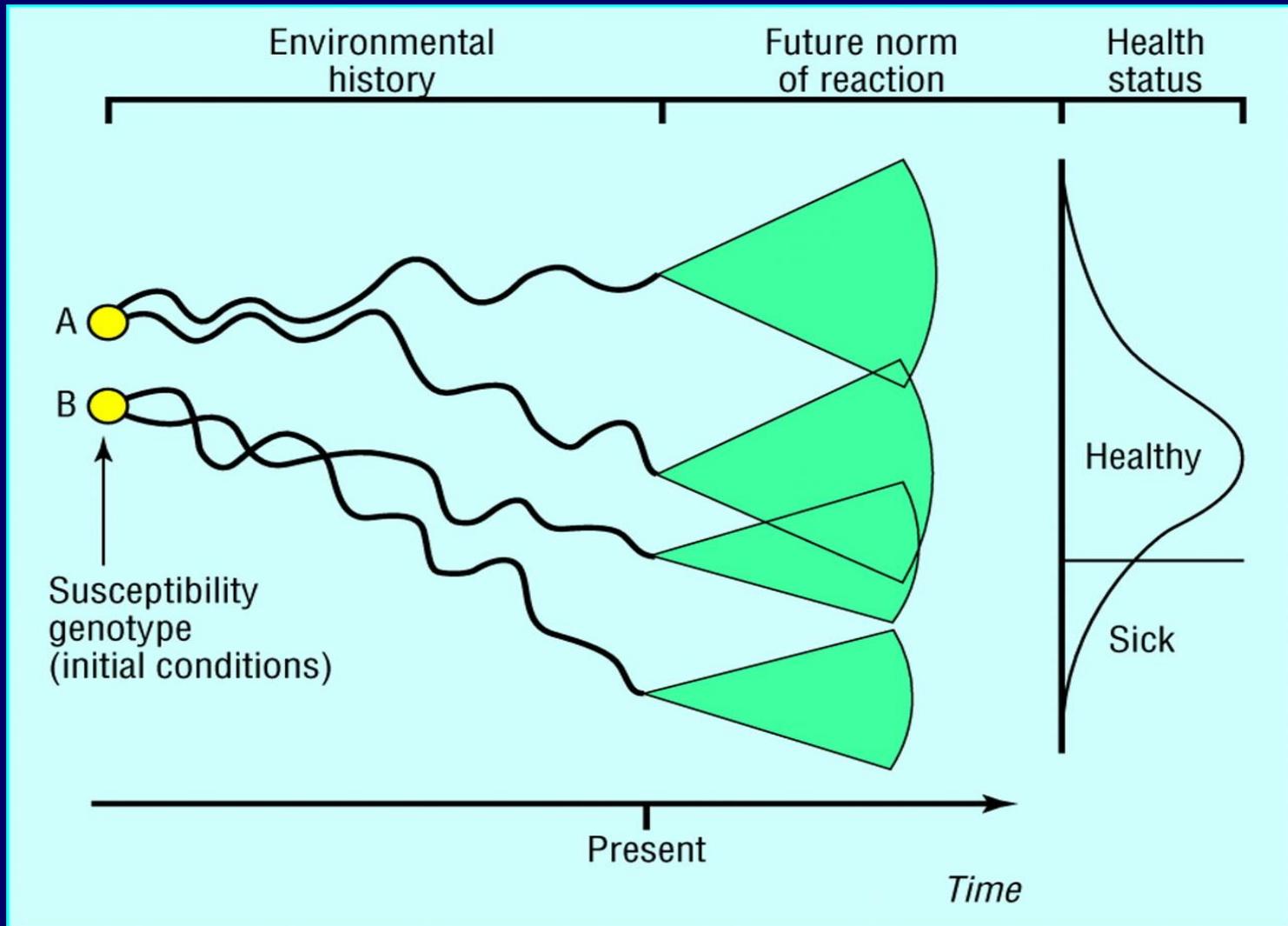
Other Environmental Items

- Remember the sun – Ultraviolet rays
- Too much in excess
 - Stress, Drugs (recreational, anabolic steroids), Diet, Traumatic events
- Too little in excess
 - Sleep, take care of your body, diet
- Eat right, sleep right, exercise, moderation

What Can We Do To Limit Exposure?

- Eat right, sleep right, stress to a minimum, take care of our bodies
- Take you medications
- Photoprotection – it really works!

Possible Genotype-Ecotype-Phenotype Associations



Twin Sibling Study

- Study of the environment's influence on rheumatic disease
- RA, SLE, Scleroderma, Myositis
- Children and Adults
- Study
 - Genetics, microchimerism, microarray
 - Environmental exposures
- Follow 5 years
- Contact Adam Schiffenbauer or Fred Miller at the NIH in Bethesda, MD

