This webinar is hosted by Kathie Madonna Swift, MS, RDN, LDN, Food As Medicine Education Director for the Center for Mind-Body Medicine, presented by Susan Blum, MD, MPH and made possible by a grant from the Scheidel Foundation.
WOMEN AND AUTOIMMUNE DISEASE

Susan Blum, MD, MPH
Founder and Director
Blum Center for Health
www.blumcenterforhealth.com
www.Blumhealthmd.com
My Story

- Hashimoto’s thyroiditis: autoimmune
- Worked through all the functional medicine testing and treatment programs to figure out how to cure it
- Within 1 year all my antibodies were gone
- Put together a program I’ve been using for over a decade with my patients
- Share with you today
4 Step Functional Medicine Program to Treat Autoimmune Disease:

1. Using Food As Medicine
2. Balancing Stress Hormones
3. Healing the Gut
4. Supporting the Liver
What we will talk about...

- **Part 1:**
  - Basics of a healthy immune system
  - The estrogen effect

- **Part 2:**
  - The role of estrogen metabolism
  - Xenoestrogens
  - Detoxification

- **Part 3:**
  - Step 1: Using Food as Medicine

- **Part 4:**
  - 4-Step Program to Treat Autoimmune Disease:
    - Step 2: Stress
    - Step 3: Healing Your Gut
    - Step 4: Liver Support for Detoxification (done in Part 2)
Autoimmune Disease

- Estimates are 25 million Americans and rising
- 2nd leading cause of chronic disease after diabetes
- Of the 50 million people living with autoimmune disease, 75% of them are women.
- 80-100 known clinically distinct diseases
  - Rheumatoid arthritis, multiple sclerosis, sjogren’s syndrome, systemic lupus erythematosis, autoimmune thyroid disease…

https://www.aarda.org/autoimmune-information/autoimmune-disease-in-women/
Eleni Tiniakou, Karen H. Costenbader, Martin A. Kriegel, Sex-specific environmental Influences on the development of autoimmune diseases, Clinical Immunology. 28 February 2013 in press
PART 1:
Foundations of a Healthy Immune System
Immune System Basics

• The immune system is divided into 2 parts:
  • **The innate immune system**: First line of defense, ready to go
  • **The adaptive immune system**: Is primed by the innate immune system, needs time to respond (hours to days), and has memory
Adaptive Immune System

Lymphocytes

B-Cells

T-Cells (naïve)

Antibodies

Cytotoxic T-Cells

T- Helpers

TH1 Promote Cytotoxic T-Cells

TH2 Promote Antibodies & B-Cells

TH17 Inflammation Autoimmunity

T REG Suppress & Regulate
Healthy Immune System

• **Th1, Th2 and Th17 turn on** appropriately and then the Immune response **turns off** when the job is done
  • **Regulator cells** are working properly
  • Th1 and Th2 are in balance, neither one dominant
• Knows the difference between self and not-self
  • Maintain **tolerance**
Autoimmunity

• Lymphocyte T helper cells are imbalanced:
  • **If Th1 is overactive:**
    • Increase in cytotoxic T cells, and less antibodies
  • **If Th2 is overactive:**
    • Increase in antibodies with less cytotoxic T cell activity
    • Immune complexes
  • When one system is “stuck on”, the other “stuck off”
    • Potential for autoimmune disease and chronic infections
  • **If Th17 is overactive:**
    • Directly causes damage to self-tissue
  • T Regulators are underactive
Autoimmune Categories

- Th1 Dominant
  - ‘Organ specific’
  - Thyroid, adrenals, pernicious anemia, autoimmune hepatitis, crohns, celiac, lichen planus, RA

- Th2 Dominant
  - ‘Systemic’
  - Lupus, scleroderma
  - ‘Immune complex’ (RA)

- Estrogen increases TH2

- There is a lot of overlap and this does not hold 100% true all the time
Estrogen effect

• Shifts to Th2: increased B cell survival and antibody production
• Also increases NK cells and cytotoxic T cells
• Stimulates inflammatory cytokines:
  • IL-1, IL-6, and TNF alpha
• Overall, estrogens show an enhancing effect on all immune responses
  • Increases susceptibility to autoimmune disease.
  • More estrogen activity in your body, greater the effect.
• Gomez A, Luckey D, Taneja V. The gut microbiome in autoimmunity: Sex matters, Clinical Immunology, Volume 159, Issue 2, August 2015, Pages 154-162.
Fig. 1. Presence of estrogen receptors in cells involved in the immune response. Functional receptors have been found at the level of macrophages, T and B cells (see red circles).

Maurizio Cutolo, Alberto Sulli, Rainer H. Straub

Estrogen metabolism and autoimmunity


http://dx.doi.org/10.1016/j.autrev.2011.11.014
PART 2

Estrogen, xenoestrogens and autoimmunity
Estrogen metabolites: weak vs strong

- **Estrogens are “detoxed” in the liver into:**
  - **2-hydroxyestrones**: mild estrogens and not carcinogenic
  - **16-alpha hydroxyestrones**: stronger than estradiol
    - can rise in response to obesity, alcohol consumption, toxic exposure, inflammation
    - High levels inked to increased risk and poorer prognosis in conditions associated with estrogen excess including lupus and cancer
  - **4-hydroxyestrones**: also stronger than estradiol
    - Most carcinogenic
    - High oxidative stress and inflammation can increase conversion of 4-estrogens to a type of estrogen called quinolones which damage DNA and increase cancer risk.

Estrogens

ENZYMATIC STEPS:
2HSD → 17α-Hydroxysteroid dehydrogenase
S9 = Steroid Reductase
CYP1A1 = 17β-Hydroxysteroid dehydrogenase
11βHSD → 11β-Hydroxysteroid dehydrogenase
CYP19A = 17β-Hydroxysteroid dehydrogenase
17βHSD → 17β-Hydroxysteroid dehydrogenase
CYP17A = 17β-Hydroxysteroid dehydrogenase
CYP19A = aromatase
CYP11A = 11β-Hydroxylase

ESTROGEN METABOLISM:
MA1 = 17β-Hydroxysteroid dehydrogenase (CYP1A1)
M1 = 17β-Hydroxysteroid dehydrogenase (CYP1A1)
COMT = Catechol-O-Methyltransferase

Enzymatic Activity

Estrogen Metabolism
2-Hydroxyestrone/16α-Hydroxyestrone Ratio

- 2-Hydroxyestrone
  - Higher risk of breast/prostate cancer
- 16α-Hydroxyestrone
  - Lower risk of breast/prostate cancer

Methylation Activity
2-Methoxyestrone/2,4-Dihydroxyestrone Ratio

- Less Methylation
- More Methylation

Interpretation

Phase 1
- 2-OHE1
- 16α-OHE1
- 2-MeO-E1

Phase 2
- 2,4-DH-E1
- 2-MeO-E1
Lupus and Estrogen Metabolism

- SLE patients tend to have higher levels of 16α-hydroxyestrone.
- It has been estimated that a 20-fold increase in the proportion of high to low potency estrogens is present in SLE patients.
- Both males and females with SLE have reduced levels of testosterone.
- Autoantibodies to ERα are present in 45% of SLE

RA and Estrogen Metabolism

- Healthy women had 10 x the amount of 2-hydroxy estrogen (good) in their urine compared to women with RA.
- The ratio of urinary 16-alpha hydroxyestrone/2-hydroxyestrogens was more than 20 times higher in RA and SLE than healthy subjects.
- In RA, just like SLE, need to focus on improving estrogen metabolism.

Birth Control Pills

• Use of combined oral contraceptives does not lead to increased flares of disease or worsening disease activity in women with inactive or stable active SLE.

• Possible increased risk of thrombosis in women with positive antiphospholipid antibodies and history of oral contraceptive use.

HRT

- Hormone replacement therapy in postmenopausal women seems to increase the risk of developing SLE.
- Studies haven’t looked at the different estrogen metabolites.
- Suggests that “in the presence of active immune-mediated diseases such as SLE (or antiphospholipid syndrome and others), B-cell dependent diseases, the administration of estrogens should be avoided”.

Treatment Goal: Reduce Estrogen Activity

- Improve metabolism of your endogenous estrogens (what you are making)
  - Lower the “bad” estrogens with food and supplements
  - I-3-C (Indole 3 Carbinole), or DIM (Di-indole-methane)
  - Methylation support: Methyl Folate and Methyl B12, SAMe

- Don’t take outside hormones like birth control pills or hormone replacement

- Avoid toxins that act like estrogens in the body: Xenoestrogens and Environmental estrogens
XenoEstrogens

• Xenoestrogens are synthetic chemical contaminants in the environment that represent a structurally diverse group of hydrocarbons with an estrogen-like activity
• universally present in the environment
  • found in food, soil, air, and water.
• major subset of endocrine disrupters
• exposure is unavoidable
XenoEstrogens

- plastics
  - (bisphenol-A, phthalates),
- detergents and surfactants
  - (octylphenol, nonylphenol),
- pesticides
  - (methoxychlor, dichlorodiphenyl-trichloroethane or DDT, hexachlorobenzene, and dieldrin)
- industrial chemicals
  - (polychlorinated biphenyls or PCBs, 2,3,7,8-tetrachlorodibenzo-p-dioxin or TCDD),
Environmental Estrogens

• Phytoestrogens or natural plant estrogens
  • genistein, coumesterol
  • soy is found in up to 60% of processed food, being a food additive and a meat substitute
• Medications
  • contraceptive pill, hormone replacement therapy, cimetidine, creams
• Food:
  • meat and dairy from hormones given to animals
  • and mycoestrogens or fungal products from *Fusarium sp.* (zearalenone).
Estrogen effects of xenoestrogens

• “Endocrine Disruptors”
• Less potent than natural estrogen (17b-estradiol)
  • BUT chemically stable, can bio-accumulate in body fat to eventually achieve a significant dose.
• Released from body fat during starvation
  • can be passed on during pregnancy or through colostrum/milk
• What do they do?
  • bind to the estrogen receptor and nuclear receptor
  • induce the synthesis of estrogen receptor-regulated proteins.
  • alter the metabolism of natural estrogens:
  • INCREASE 16α-hydroxyestrone
The immune system as a potential target for environmental estrogens (endocrine disrupters): a new emerging field

Sattar Ansar Ahmed *
Center for Molecular Medicine and Infectious Diseases, Department of Biomedical Sciences and Pathobiology, 1410, Prices Fork Road, Virginia Maryland Regional College of Veterinary Medicine, Virginia Tech (Virginia Polytechnic Institute and State University), Blacksburg, VA 24060, USA

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Abstract

It is now well known that natural (17β-estradiol) and synthetic (e.g. diethylstilbestrol) estrogens not only affect the reproductive system, but also markedly influence the immune system. Recently, a new class of estrogens that is abundant in the environment (in industrial chemicals, pesticides, and surfactants) has been recognized. Some of these estrogenic chemicals (which are a large subgroup of endocrine disrupters) have also been shown to influence the immune system. This review assimilates growing evidence in wildlife, laboratory animals and to a limited extent in humans, which suggests that environmental chemicals may also affect the immune system. Further studies are needed to ascertain the immunological consequences of exposure to environmental estrogens, especially in humans. At the present time, it is not known whether the human immune system responds to a low dose of environmental estrogens or if environmental estrogens influence certain subsets of human populations, rather than the general population. Conceivably, an alteration of the immune system by environmental estrogens could affect the individuals’ ability to mount well-regulated immune responses to microbial and vaccine antigens, allergens, self and tumor antigens. Possible changes in the immune system must be investigated routinely in toxicity studies. A comprehensive mechanistic understanding of potential immunomodulatory chemicals is needed. In this regard, relevant laboratory animals may be especially useful in identifying susceptible periods of life, whether both genders are equally affected, in analysis of changes in target lymphoid organs, and to determine the immunological effects of mixtures of chemicals. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Immune; Autoimmune; Estrogens; Environmental estrogens; Endocrine disrupters; Allergies

1. Introduction

Two relatively recent conceptual advances in endocrinology are noteworthy. The first is the recognition that sex hormones are not merely ‘reproductive hormones’. Rather, they affect the functioning of several non-reproductive tissues, notably the immune system. The second conceptual advance is that estrogens exist not only as natural or synthetic compounds, but also as environmental estrogens.
Exposure to PCBs linked to RA: in a 2007 cross-sectional study, serum concentration of PCBs was positively associated with a self-reported diagnosis of RA.

Insecticide Use and Risk of Rheumatoid Arthritis and Systemic Lupus Erythematosus in the Women’s Health Initiative Observational Study

CHRISTINE G. PARKS, 1 BRIAN T. WALITT, 2 MARY PETTINGER, 3 JIU-CHUAN CHEN, 4 ANNECLAIRE J. DE ROOS, 3 JULIE HUNT, 3 GLORIA SARTO, 5 AND BARBARA V. HOWARD 6

Objective. Farming and agricultural pesticide use has been associated with 2 autoimmune rheumatic diseases, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). However, risk associated with other residential or work place insecticide use is unknown.

Methods. We analyzed data from the Women’s Health Initiative Observational Study (n/H11549 76,861 postmenopausal women, ages 50–79 years). Incident cases (n/H11549 213: 178 for RA, 27 for SLE, and 8 for both) were identified based on self-report and use of disease-modifying antirheumatic drugs at year 3 of followup. We examined self-reported residential or work place insecticide use (personally mixing/applying by self and application by others) in relation to RA/SLE risk, overall and in relation to farm history. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were adjusted for age, race, region, education, occupation, smoking, reproductive factors, asthma, other autoimmune diseases, and comorbidities.

Results. Compared with never used, personal use of insecticides was associated with increased RA/SLE risk, with significant trends for greater frequency (>6 times/year) and duration (>20 years). Risk was also associated with long-term insecticide application by others (HR 1.85, 95% CI 1.07–3.20 for >20 years) and frequent application by others among women with a farm history (HR 2.73, 95% CI 1.10–6.78 for >6 times/year).

Conclusion. These results suggest residential and work place insecticide exposure is associated with the risk of autoimmune rheumatic diseases in postmenopausal women. Although these findings require replication in other populations, they support a role for environmental pesticide exposure in the development of autoimmune rheumatic diseases.

INTRODUCTION

Autoimmune rheumatic diseases (ARDs) such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) affect as many as 1.6 million adults in the US (1) and disproportionately impact women, the elderly (RA), and minorities (SLE) (2–4). Established risk factors include family history of autoimmune disease and genetic characteristics. Like most complex diseases, the etiology of ARD is also influenced by environmental exposures. However, knowledge of specific environmental risk factors is limited (5), with most evidence of associations pertaining to smoking and various occupational exposures (6,7).

The occupation of farming has been associated with ARD in different populations and using different study designs, with several studies suggesting a role of pesticide exposure from farming (8–12). One recent study reported an association between farming occupation and death with
What can you do? Detox Your World

**Avoid Xenoestrogens:**
- Plastics: use glass containers.
- Solvents: cleaning supplies in your home
- Parabens: read labels on cosmetics
- Herbicides/Pesticides: lawn care, organic food
- Processed food: animal and vegetable

**Detox your body and your estrogens:**
- Liver support detox program
  - Include DIM and methylation support supplements
- Start with Food!
PART 3: STEP 1: USING FOOD AS MEDICINE

Detoxification of estrogens
Reduce oxidative stress
Support gut microbiome
Anti-inflammatory Food Plan

- Remove the “bad stuff”
  - Sugar, high glycemic processed carbs
  - Trans fats, hydrogenated oils, processed oils. Limit saturated animal fat
  - Poor quality protein: feedlot cows, farmed and high mercury fish, all animals given antibiotics and hormones
  - Food dyes, chemicals, preservatives
  - For autoimmunity: gluten free diet.
  - Consider removing high lectin food: legumes and grains
  - Begin with elimination diet to test for food sensitivities: dairy, soy, corn, eggs. Nightshades if arthritis (tomato, potato, eggplant, peppers)
Best food choices

• Focus on the “good stuff”
• Support:
  • Estrogen metabolism
  • Liver detoxification
  • Gut microbiome
• Reduce:
  • Inflammation: healthy fats like olive oil and omega 3’s
  • Oxidative stress with antioxidants
  • Diabetes and cardiovascular disease with lots of fiber and plants
Support Estrogen Metabolism

• Food:
  • Soy, EFA’s, flax, other phytoestrogens
  • Cruciferous veggies, antioxidants
  • Organic: pesticide avoidance

• Supplements: related to compounds found in cruciferous vegetables
  • Indole-3-Carbinol (I3C)
  • DIM: diindolemethane
  • Sulforaphane
Nature Reviews Cancer 3, 768-780 (October 2003)
Support Liver Detox System

• First lower toxic load:
  • Reduce exposure: Clean up environment:
    • food, water, air, cosmetics, household cleaners, etc.

• Support liver metabolic detoxification
  • Antioxidants!
  • Minerals
  • B vitamins- methylation
  • Amino acids, essential fatty acids

• Remember, estrogens are metabolized in the liver!
  • We call it estrogen detox
  • All nutritional support for your liver detox system will help your estrogens
Liver detoxification pathways and supportive nutrients
Oxidative stress

• Many studies show people with RA have high amounts of oxidative stress in both their joints and body-wide
  • Too many free radicals and not enough antioxidants
  • Increases aromatase activity
• Low levels of antioxidants:
  • Vitamin A, C, E
  • Glutathione
  • Beta carotene
• Need to replenish antioxidants in autoimmune disease
  • Helps treat inflammation and prevent tissue damage
  • Helps liver detox process

Antioxidants

- Antioxidant-rich foods: all colorful fruits and vegetables filled with phytonutrients! Nature gave us an abundance.
- Eat many different colors every day.
- Supplementation might be necessary, but should be temporary.
Support Gut Health with Food

• 70% of immune system develops in your gut
• Dysbiosis and leaky gut are associated with autoimmune disease
• Must heal the gut as foundation for treating autoimmunity
• **Food: #1 most powerful influence on your gut microbes**
  • High fiber, polyphenol rich, whole foods, plant based diet
    • Mediterranean and Vegetarian diets are most well studied for promoting good gut health
  • Cultured and fermented foods: probiotics are immunomodulators!
  • Limit: processed food, sugar, alcohol, animal protein and fat.
“How are you not seeing this? Of course doughnuts are a hole food!”
PART 4: IMMUNE SYSTEM RECOVERY PLAN

Quick summary of 4 Step Program to Treat Autoimmunity
The 4-Step Program for Treating Autoimmune Disease:

- Fix the Immune Foundations
  - **Step 1: Food**: Gluten free, elimination of food sensitivities, anti-inflammatory diet
  - **Step 2: Stress**: Balance stress hormones and heal adrenals
  - **Step 3: Gut**: Restore beneficial flora and heal gut lining
  - **Step 4: Detox**: Remove source of toxic load on the immune system and support detoxification in the liver

- FREE downloads for all 4 steps:
  - [https://blumhealthmd.com/the-immune-system-recovery-plan/](https://blumhealthmd.com/the-immune-system-recovery-plan/)
Hormone Orchestra

- All hormones are connected
- Stress: lowers progesterone levels and makes Estrogen more dominant in the body
  - Includes lack of sleep and physical stress, in addition to emotional
- Cortisol: too much is bad for autoimmunity
  - Shifts immune system to TH2, like estrogen, and negatively effects your gut flora:
- You can’t always avoid external stressors, but you can change your stress response.
  - Meditation or other relaxation practice:
    - Trains the mind and the body to stay calm when triggered
    - Turns off the stress response daily so the body can recover and balance
    - Provides insight and awareness for next steps in your journey
Dysbiosis

- Imbalance in microbe population of the gut
- Can be overgrowth of harmful bacteria, yeast or parasites
- And/or too little good bacteria
- May or may not have gut symptoms
- Caused by:
  - Stress
  - Antibiotics
  - PPI’s and antacids
  - Gut infections
  - Diet
- **Dysbiosis can lead to Leaky Gut**
What is a leaky gut?

- Intestinal Barrier: the functioning separation of the gut lumen from the host.
  - Mechanical, humoral, immune, muscular and neurological elements
- **Impaired** Intestinal Permeability = **Leaky Gut**
- **Leaky gut is associated with autoimmunity:**
  - If you have an autoimmune condition, assume you have a leaky gut.
What Causes Leaky Gut?

- Dysbiosis
- Medication: steroids, antacids, PPI’s, advil
- Alcohol
- Antibiotics
- STRESS
- Acute trauma: emotional or physical
- Toxins
- Infections
Healing Your Gut: Fix the Flora

• Treat dysbiosis and improve the microbiome balance is the first goal of treatment
• Giving probiotics isn’t enough for remission
• Functional Medicine 5 R GUT program
  • Remove: bad food and harmful microbes
  • Replace: digestive enzymes, bile, stomach acid
  • Reinoculate: the good bacteria
  • Regenerate: a healthy intestinal lining/barrier
  • Retain: long term health and resiliency
• HealMyGut program on blumhealthmd.com:
  • https://blumhealthmd.com/program-page/
Terroir de Gut

• Recommendations based on experience
• For long term gut health, focus on the ‘soil’
• Nutrition: vegetable based diet rich in prebiotic fiber
• Identify and lessen all the damaging behavior:
  • Stress: direct effect on gut micro-environment
  • Ingested Toxins
  • Alcohol
  • Medication: PPI’s, antacids, steroids, NSAIDS
• Oral microbiome: bacteria seed the gut
Free downloads with food plans and assessments:
https://blumhealthmd.com/the-immune-system-recovery-plan/

Free Immune Recovery Masterclass: Sept 25th:
Register here: https://blumhealthmd.com/immunemasterclass

8-Week Immune Recovery Challenge: October 16th:
https://blumhealthmd.com/
If you do not change direction, you may end up where you are heading.”

--Lao Tzu
This webinar has been recorded. The presentation and the slides will be available within 24 hours at CMBM.org/webinar.
Food As Medicine
for Women’s Health

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Esalen Institute
Big Sur, CA

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