

Unravelling the Mysteries of Autoimmunity



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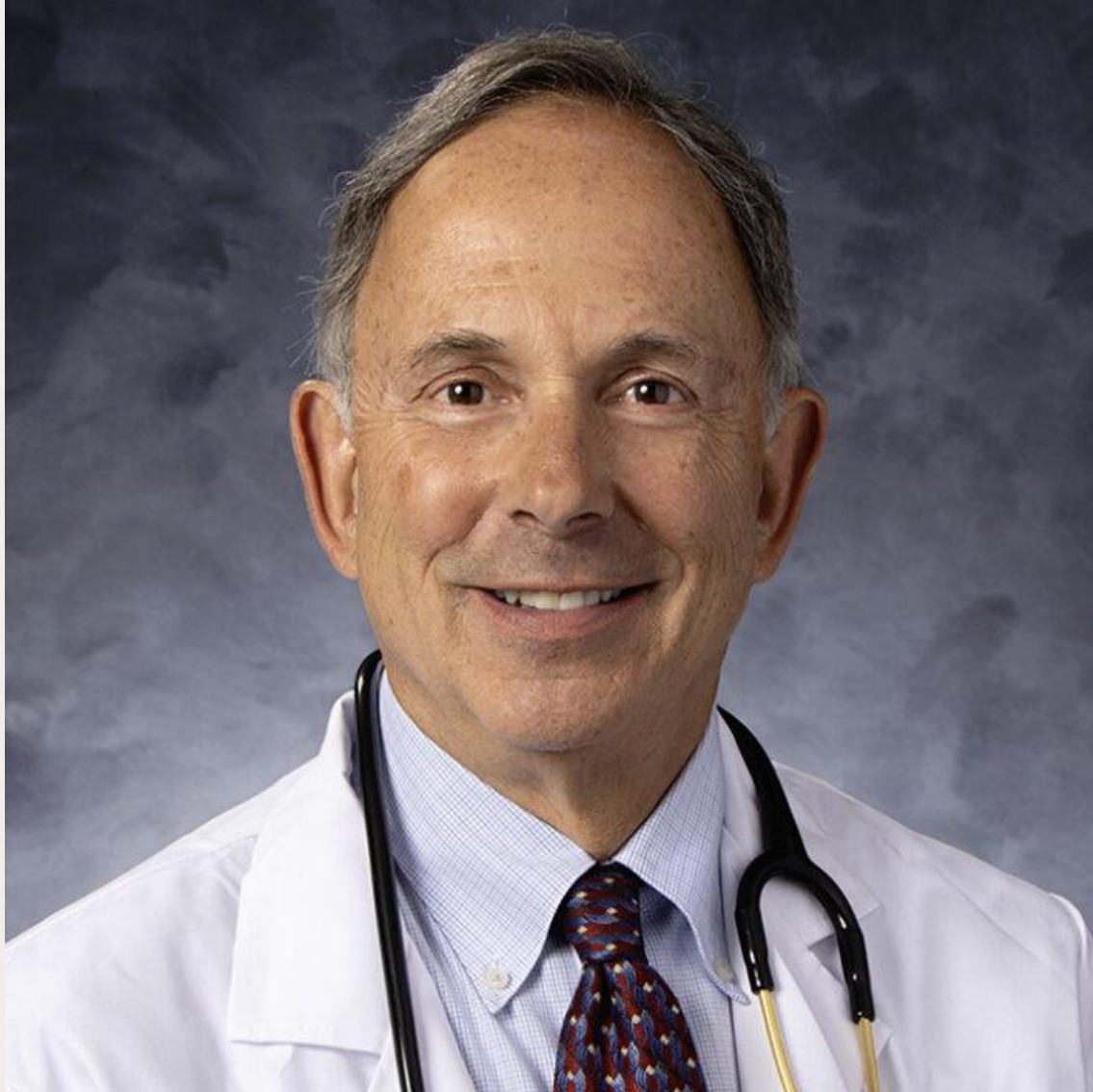
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Medical Director

Monadnock Rheumatology Associates



About Me



I bring a wealth of experience as an expert Rheumatology clinician and accomplished researcher with over 30 years of experience. Before joining MCH, I served as Rheumatology Section Chief for Memorial Health System in Marietta, Ohio, and was Chairman of Medicine for Adirondack Health Systems. I also served as the Chief Medical Officer of the Trudeau Institute, both in Saranac Lake, New York, as well as was President and CEO of Berkshire Rheumatology Associates in Pittsfield, MA for decades, among other clinical leadership positions.

“I prefer to adopt a holistic perspective in patient care, whether it be a combination approach to inflammatory polyarthritis (NSAIDs, DMARDs, Biologics, glucocorticoids) or behavioral change incorporating weight reduction, gabapentanoids, SSRIs and other adjuvant therapies used to change self-perception and pain thresholds which are life limiting. I work closely with the other medical specialties including dermatology, pulmonary and renal medicine, and emphasize clear communication and appreciation of alternative approaches to problem-solving. I look forward to serving the Monadnock Region.”



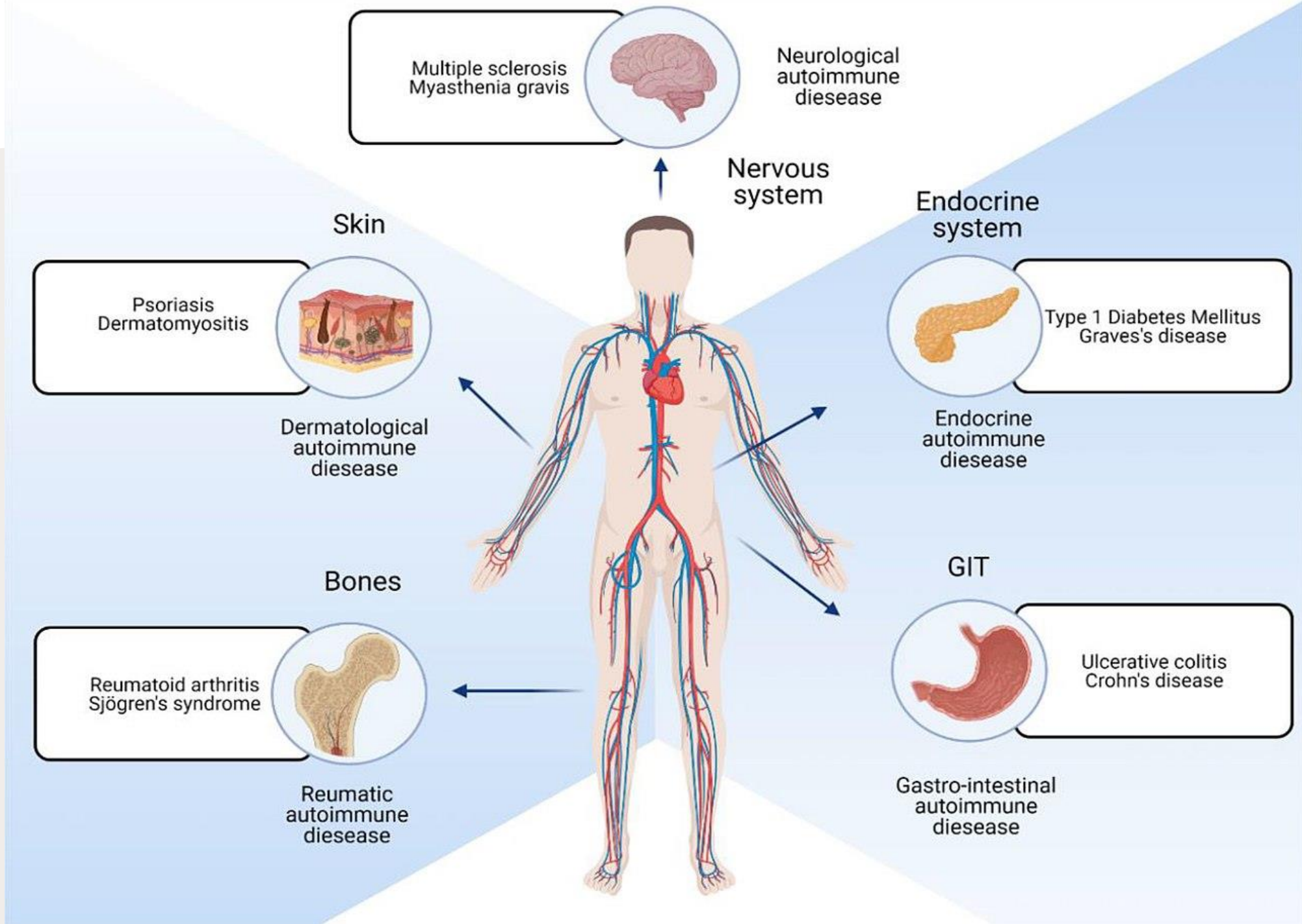
Autoimmunity: "A system of immune responses of an organism to itself"

Examples of Autoimmune Dysregulation:

- Diabetes Mellitus Type 1
- Hashimoto's Thyroiditis
- Rheumatoid Arthritis
- Systemic Lupus
- Sjogren's Syndrome

Working Definitions:

- **Tolerance** - The ability of a body to ignore self when reacting to a foreign invader
- **Loss of tolerance** - an aberrant response which targets both invading pathogens and one's own body
- **Immunodeficiency** - The decreased ability of an organism to clear an infection. This results in perpetual immune system activation

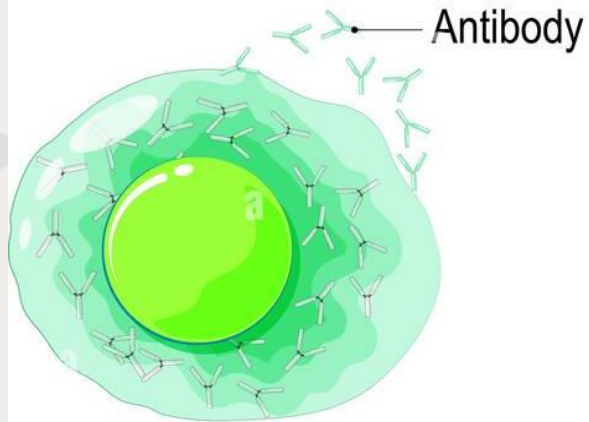
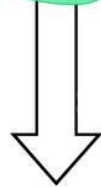


Adaptive Immunity

- 1. Encounter.** An unknown substance (protein, irritant, antigen) enters the body
- 2. Activation.** T cells identify the invader, differentiate and proliferate
- 3. Attack.** T helper cells produce small molecules (cytokines) which stimulate and transform B cells. Some B cells form antibody-secreting plasmablasts
- 4. Memory.** Some T and B cells will persist after primary exposure to antigen

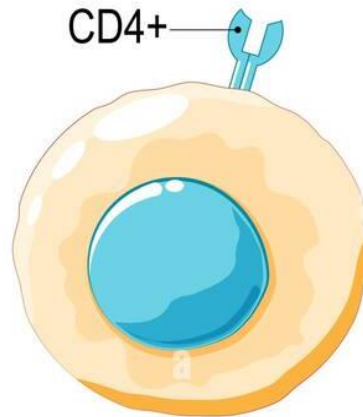
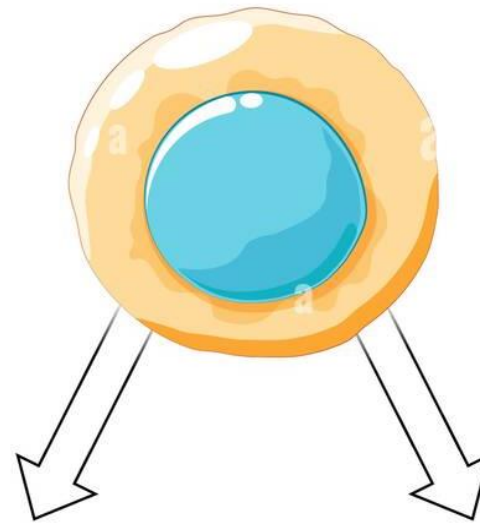
Lymphocytes

B cell
(humoral immunity)

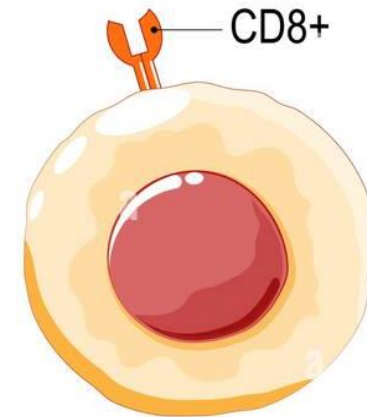


Plasma cell

T cell
(adaptive immune response)



T helper



T-killer

Examples of Autoimmune Disease

Systemic Lupus Erythematosus

- **Unknown Ag triggers** Th cell response
- **Cytokines** (TNF, IL-1, IL-6, others are released which stimulate B cells)
- **Antibodies to DS DNA** are released which bind plasma complement
- **Clinical features explode** – these include rash, fatigue, joint pain and major organ damage secondary to immune complex deposits

The Faces of Lupus



Rheumatoid Arthritis

1. Symmetric, autoimmune polyarthritis affecting small joints of the hands, wrists and feet
2. Frequently accompanied by nodule formation over the MCPs, wrists and elbows
3. Commonly associated with IgM rheumatoid factor (RF positivity) and anti-CCP autoantibody
4. Many syndromes:
 - Felty's (RA, splenomegaly, neutropenia)
 - Kaplan's (RA, pulmonary nodule formation)
 - Rheupus (RA and SLE)

Rheumatoid Arthritis in Hands



Disease Classification

1. Does the patient satisfy criteria for the disease?
2. Moving picture vs. Static image
3. Diagnostic certainty or hypothesis testing
4. Confirmation vs. 'weight of evidence'

Therapeutic Approaches

Always disease-specific

Inhibition of T-cell activation

Blocking cytokine release

B-cell depletion

Binding pathogenic autoantibodies

Patient considerations

- Oral, SQ or IV dosing
- Cost of therapy
- Duration of treatment
- Potential toxicity

Pharmacoeconomics

- Pricing of emerging therapies
- Biosimilars and genericization
- Manufacturer's assistance
- Foundational support

Clinical trials

Selection of candidates

Amelioration of cost

Evolving algorithms of care

Examples of Disease Management

Systemic Lupus Erythematosus

Mild Disease (Joint pain, fatigue, alopecia, malar rash, positive ANA)

Plaquenil, NSAIDs, low dose steroids

Moderate Disease (Above plus renal, pulmonary, hematologic, CV and CNS features) Pulse steroids, Imuran, MMF, Voclosporin, Saphnelo, Benlysta

Severe (Major organ dysfunction including all the above)

Rituxan or Cytoxan plus pulse steroids and the above

Rheumatoid Arthritis

Mild Disease (joint pain, morning stiffness, generalized fatigue)

- Low dose prednisone, NSAIDs, topical therapy

Moderate to Severe Disease (synovitis, nodulosis, deformities)

- Methotrexate, MMF, Plaquenil, Imuran, tapering steroids
- TNFs, JKs, IL-1's, IL-6's, Costimulation blockers, Rituxan (if DMARDs are ineffective after 12 weeks)

Other Challenges

- **Scleroderma** (limited vs diffuse systemic)
- **Sjogren's** with interstitial pulmonary fibrosis and/or B cell lymphoma
- **Idiopathic inflammatory muscle** (polymyositis, dermatomyositis, inclusion body)

Novel Mechanisms

- FCRNs (neonatal Fc receptor antagonists)
- Anti-CD40/CD40L
- CAR T CD19 (autologous and allogenic approaches)
- Bispecific antibodies (CD19x CD3)



Questions?



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