

Autoimmune Diseases

Course Description

"Autoimmune Diseases" is an online recorded video of a previously presented live CE webinar for rehabilitation professionals. This course presents contemporary information about four of the most common autoimmune diseases: type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus. This course includes discussion of pathophysiology, etiology, clinical presentation, and therapeutic management strategies.

Course Rationale

The purpose of this course is to provide participants with contemporary information about four of the most common autoimmune diseases. Rehabilitation professionals can use this information to develop and implement effective treatment programs that address the specific needs of individuals effected by these disorders.

Course Goals and Objectives

Upon completion of this course, participants will be able to:

1. Compare normal and dysfunctional immune system functioning.
2. Distinguish the primary mechanisms of tissue damage in autoimmune disease.
3. Identify etiological factors contributing to the development of autoimmune disease.
4. Differentiate organ and system specific autoimmune diseases.
5. Identify the immunologic mechanisms contributing to multiple sclerosis, type 1 diabetes, rheumatoid arthritis, and systemic lupus erythematosus.
6. Describe the clinical presentation of common autoimmune conditions.
7. Identify therapeutic considerations for common autoimmune conditions.
8. Identify pharmacological trends for common autoimmune conditions.
9. Identify other common autoimmune diseases and comorbidities.
10. Identify emerging trends in the management of autoimmune diseases.

Course Provider – Innovative Educational Services

Course Instructor - Jodi Gootkin, PT, MEd, CEAS

Target Audience – PTs, PTAs, OTs, OTAs

Course Educational Level – This course is applicable for introductory/intermediate learners.

Course Prerequisites – None

Method of Instruction/Availability – Recorded video available on demand at cheapceus.com.

Criteria for Issuance of CE Credits – Completion of viewing of 3 hour recorded video, and a score of 70% correct or greater on the course post-test

Continuing Education Credits – Three (3) hours of continuing education credit.

Course Fee - \$34.95

Conflict of Interest – No conflict of interest exists for the presenter or provider of this course.

Refund Policy - Unrestricted 100% refund upon request. The request for a refund by the learner shall be honored in full without penalty or other consideration of any kind. The request for a refund may be made by the learner at any time without limitations before, during, or after course participation.

Course Outline

- The Healthy Immune System
- Immune System Dysfunction
- Etiology
- Type I Diabetes Mellitus
- Multiple Sclerosis
- Rheumatoid Arthritis
- Systemic Lupus Erythematosus
- Other Autoimmune Diseases & Comorbidities
- Emerging Therapeutic Trends
- Discussion of Clinical Applications

Autoimmune Diseases

Live Interactive Webinar
Presented By:

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Course Rationale

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Goals and Objectives

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5. Identify the immunologic mechanisms contributing to multiple sclerosis, type 1 diabetes, rheumatoid arthritis, and systemic lupus erythematosus.
6. Describe the clinical presentation of common autoimmune conditions.
7. Identify therapeutic considerations for common autoimmune conditions.
8. Identify pharmacological trends for common autoimmune conditions.
9. Identify emerging trends in the management of autoimmune diseases.
10. Identify contemporary dietary considerations in the management of autoimmune diseases.

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Disclaimer

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Application of concepts presented in this webinar is at the discretion of the individual participant in accordance with federal, state, and professional regulations.

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Healthy Immune System

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- Humeral Immunity: B-cells recognize antigens attacking them and retaining memory with antibodies engaging for protection with subsequent exposure.
- Cellular Immunity: T-cells promote long term immunity through
 - Cytotoxic T-cells disrupt cell membrane, target cell's DNA, and to destroy invading cells
 - Regulator T-cells (Tregs) inhibit T and B cells to prevent self injury and maintain tolerance

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Immune System

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- Collectively, autoimmune diseases are among the most prevalent diseases in the US, affecting more than 23.5 million Americans.

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Self-tolerance

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- A complex network protects against foreign agents (antigens) and removes apoptotic cells.
- The sophisticated process itself does not induce an immune response as the body recognizes its own tissues which is referred to as self-tolerance.

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Immune System Dysfunction

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- Hypersensitivity**
 - Allergic reaction
- Immunodeficiency**
 - Immune system unable to suppress foreign antigens
- Autoimmune Disease**
 - Loss of self-tolerance causes an amplified autoimmune response
 - Autoantigens – normal tissue that is targeted by humeral or cell-mediated immune response

Consider This

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Pathophysiology of Autoimmune Diseases

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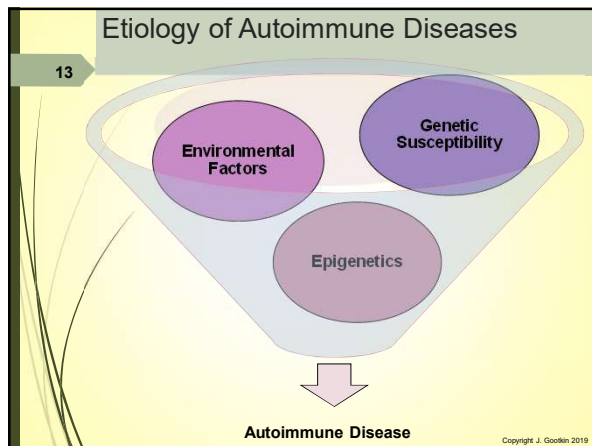
Without elimination of the stimulating antigen, a self-perpetuating response of effector pathways leads to a chronic inflammatory immune-mediated response and tissue damage.

```

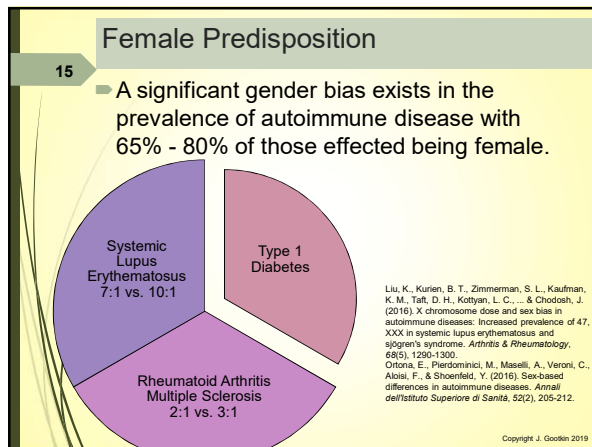
graph TD
    A[Autoantigen present] --> B[Adaptive immune response]
    B --> C[Effector mechanism directed at body]
    C --> D[Amplified immune response]
    D --> E[Autoantigen remains present]
    E --> A
  
```

Consider This

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- ### Genetic Susceptibility
- 14
- Major Histocompatibility Complex (MHC) specifically the Human Leukocyte Antigen (HLA) genes supply the instructions for synthesis of critical immune system proteins.
 - Alterations appear to create T-cell dysfunction allowing them to become more autoimmune reactive.
 - Genetic mapping has noted specific genetic variants that predispose individuals to multiple autoimmune diseases suggesting common pathogenesis.
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- ### Female Predisposition Continued
- 16
- Immune cells contain receptors for estrogens, progesterone, androgens and prolactin that influence their functioning.
- | | |
|--|---|
| Estrogens
Enhance immunity
Exacerbate autoimmunity | Testosterone and Progesterone
Immunosuppressive
Protect against self-attack |
|--|---|
- During early female embryogenesis, one of the two X chromosomes is silenced but some immune related genes may escape inactivation allowing overexpression of autoantigens.
- Ortona, E., Pierdominici, M., Maselli, A., Veroni, C., Aloisi, F., & Shoenfeld, Y. (2016). Sex-based differences in autoimmune diseases. *Annali dell'Istituto Superiore di Sanità*, 52(2), 205-212.
- Chifris, S., Monteiro, J., Glass, D., Apatoff, B., Salmon, J., Concannon, P., & Gregersen, P. K. (2000). The role of X-chromosome inactivation in female predisposition to autoimmunity. *Arthritis Research*, 2(5), 399-406. Copyright J. Gootkin 2019

- ### Epigenetics
- 17
- Emerging research is identifying the processes that help direct when individual genes are turned on or off.
 - These influence cellular function without altering the DNA and may be triggered by environmental influences.
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- ### Environmental Factors
- 18
- Specific triggers may activate genes with the development autoantibodies initiating the pathologic process.
 - Food additives
 - UV exposure
 - Infectious agents
 - Chemical toxins
 - Tobacco smoke
 - Stress
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Food Additives

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- The gut contains a significant proportion of the body's immune cells with the intestinal microbiota playing a role in immune homeostasis.
- The tight mucosal intercellular junctions balance regulatory and effector T-cell action in response to antigens.
- Diet can substantially effect this equilibrium and structure which in turn increases proinflammatory cytokines, reduced Tregs responsiveness, and susceptibility to autoimmune inflammation.

Campbell, A. W. (2014). Autoimmunity and the Gut. *Autoimmune Diseases*, 2014, 152428. <http://doi.org/10.1155/2014/152428>. Copyright J. Gootkin 2019

Food Additives Continued

20

- Certain food additives increase the intestinal mucosal permeability allowing exposure to foreign immunogenic antigens that trigger the autoimmune cascade.
 - Glucose
 - Salt
 - Emulsifiers
 - Gluten
 - Transglutaminase
 - Nanoparticles

Lerner, A., & Matthias, T. (2015). Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease. *Autoimmunity Reviews*, 14(6), 479-489. Copyright J. Gootkin 2019

Vitamin D Deficiency

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- Vitamin D receptors (VDR) on target organs allow mineral metabolism which contributes an immune modulating effect to the body.
- Mutations on the VDR gene that encode the receptors is associated autoimmune disease.
- It is proposed that the resultant low levels of Vitamin D are a causative factor in the development of autoimmune disease.

National Center for Biotechnology Information. (2017) VDR Vitamin D receptor [Homo sapiens (human)] Gene ID: 7421 Updated Sept 17, 2017. <https://www.ncbi.nlm.nih.gov/gene/7421#summary>
 Hayes, C. E., Hubler, S. L., Moore, J. R., Barta, L. E., Praska, C. E., & Nashold, F. E. (2015). Vitamin D actions on CD4+ T cells in autoimmune disease. *Frontiers in Immunology*, 6, 100. Copyright J. Gootkin 2019

Vitamin D Deficiency Continued

22

- Ultraviolet light exposure is the primary method of Vitamin D production.

Hart, P. H., Gorman, S., & Finlay-Jones, J. J. (2011). Modulation of the immune system by UV radiation: more than just the effects of vitamin D? *Nature Reviews Immunology*, 11(9), 584-596. Copyright J. Gootkin 2019

Vitamin D Deficiency Continued

23

- A strong latitudinal gradient exists for Multiple Sclerosis and Type 1 Diabetes where higher geographic latitude is associated with increased disease prevalence.

Noonan CW, Williamson DM, Henry JP, Indian R, Lynch SG, Neuberger JS, et al. The prevalence of multiple sclerosis in 3 US communities. *Prev Chronic Dis* 2010;7(1):A12.
 Simpson S, Blizzard L, O'Leah P, et al Latitude is significantly associated with the prevalence of multiple sclerosis: a meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry* 2011;82:1132-1141. Copyright J. Gootkin 2019

Developmental Origins of Health and Disease (DOHAD)

24

- Previously referred to as Fetal Origins Of Adult Disease (FOAD) or Baker Hypothesis
- Theory proposes that maternal environmental exposures are alter the intrauterine environment influencing fetal tissue structure which can predispose to the development of disease later in life.
- An inverse relationship has been found between UVB exposure during gestation and development of adult autoimmune disease.

Disanto, G., Chaplin, G., Morahan, J. M., Giovannoni, G., Hyppönen, E., Ebers, G. C., & Ramagopalan, S. V. (2012). Month of birth, vitamin D and risk of immun-mediated disease: a case-control study. *BMC medicine*, 10(1), 69. Copyright J. Gootkin 2019

25 Chemical Exposure

- Silica dust exposure primarily leads to silicosis lung disease with increased production of autoantibodies and immune complexes also noted.
- Associations with other autoimmune diseases is emerging.
 - Systemic Lupus Erythematosus
 - Rheumatoid Arthritis

Shtrachman, O., Blanc, P. D., Ollech, J. E., Fridel, L., Fuks, L., Fireman, E., & Kramer, M. R. (2015). Outbreak of autoimmune disease in silicosis linked to artificial stone. *Occupational Medicine*, kqy073. Copyright: J. Gootkin 2019

26 Classification of Autoimmune Diseases

- As the etiology is not specifically understood, classification is based on patterns of presentation and the specific cells involved in the immune responses.
- Type III Immune Complex Response
 - Systemic
 - Systemic Lupus Erythematosus
 - Rheumatoid Arthritis
 - Type IV T-cell Response
 - Organ-specific
 - Type I Diabetes
 - Multiple Sclerosis

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27 Type III Immune Complex Disease

- In a normal response, antibodies bind to the foreign substance creating large immune complexes when there are enough antibodies that are subsequently cleared by the reticuloendothelial system.
- When more ubiquitous autoantigens are present than IgG antibodies, small immune complexes form which are deposited in tissues and small blood vessels.
- Rheumatoid Arthritis
 - Rheumatoid Factor, Tumor Necrosis Factor (TNF) cytokine
- Systemic Lupus Erythematosus
 - DNA, histones, ribosomes, snRNP, scRNP

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28 Type IV T-cell Mediated Disease

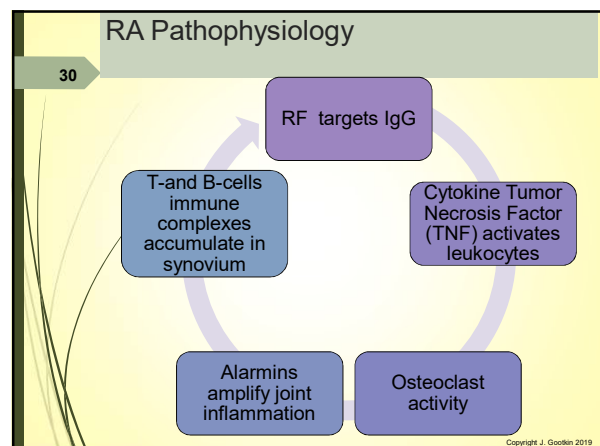
- Organ-specific damage results directly from T-cell actions against the tissues or failure of regulatory T-cells (Tregs) to limit the inappropriate inflammatory response.
- Multiple Sclerosis
 - Myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein
- Type I Diabetes Mellitus
 - Pancreatic beta cell destruction

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29 Rheumatoid Arthritis (RA)

- Altered T-cell activation and production of Rheumatoid Factor (RF) autoantibodies target a portion of the naturally occurring IgG antibody.
- The immune complexes produced provoke activation of synovial leukocytes stimulating an intense inflammatory process.
- Chronic inflammation leads to progressive synovial deterioration, hyperplasia, joint erosion and systemic symptoms of the cardiovascular and pulmonary systems.

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RA Diagnosis

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- Laboratory tests measure inflammation and biomarkers.

Inflammation	Antibodies
Erythrocyte Sedimentation Rate (ESR)	Rheumatoid Factor (RF)
C-Reactive Protein (CRP)	Anti-Cyclic Citrullinated Peptide (anti-CCP)
	Antinuclear Antibody (ANA)

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RA Clinical Presentation

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- Characterized by polyarticular pain, morning stiffness, fatigue, restricted range of motion, joint deformity, and joint inflammation.
 - Bilaterally primarily small joints affected
 - Exacerbations and remissions

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RA Joint Deformities

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Boutonniere	<ul style="list-style-type: none"> MCP Hyperextension PIP Flexion DIP Hyperextension
Swan Neck	<ul style="list-style-type: none"> PIP Hyperextension DIP Flexion
Hitchhiker's Thumb	<ul style="list-style-type: none"> MCP Flexion IP Hyperextension
Ulnar Drift	<ul style="list-style-type: none"> MCP joints sublux with fingers shifting toward ulna
Claw Toe	<ul style="list-style-type: none"> MTP Hyperextension PIP and DIP Flexion

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RA Complications

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- Some patients experience systemic extra-articular complications from RA.
 - Anemia
 - Rheumatoid nodules in skin
 - Lung Fibrosis
 - Renal Amyloidosis
 - Atherosclerosis
 - Low Vision
 - Peripheral Neuropathy
 - Osteoporosis

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RA Medical Management

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- Comprehensive management of RA includes:
 - Monitoring for long term system compromise
 - Dietary modification
 - Rehabilitation
 - Pharmacologic agents
 - Joint replacement surgery

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RA Dietary Modification

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- EPA and DHA are Omega-3 fatty acids that decrease pro-inflammatory cytokine production, contribute to deactivation of B-cells and synoviocytes.
 - Improved morning stiffness, pain levels, and joint inflammation have been noted.
 - Marine based Omega-3 show best results

Tedeschi, S.K. & Costenbader, K.H. Is there a role for diet in the therapy of rheumatoid arthritis? *Current Rheumatology Report* (2016) 18: 23.
Lemerle, J., Arfeevskaya, M. I., Brooks, W. H., & Renaudineau, Y. (2016). Effects of enviro environmental factors and omega-3 fatty acids on rheumatoid arthritis. *Annals of Joint*, 1(4).

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37 RA Rehabilitation Considerations

- Strengthening provides stability to affected joints – isometric exercise for inflamed joints.
- ROM and contracture management – avoid stretching acutely inflamed joints.
- Education on energy conservation and joint protection.
- Centers for Disease Control and Prevention Arthritis Programs
 - Physical Activity
 - Self-Management

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38 RA Assessment Tools

- American College of Rheumatology endorses specific tools to assess disease activity and define remission.
- Disease Activity Score (DAS28)
- Patient Activity Scale (PAS)
- Routine Assessment of Patient Index Data 3 (RAPID3)
- Clinical Disease Activity Index (CDAI)
- Simplified Disease Activity Index (SDAI)

Anderson, J., Caplan, L., Yazdany, J., Robbins, M. L., Neogi, T., Michaud, K., ... & Kazi, S. (2012). Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. *Arthritis care & research*, 64(5), 640-647.

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39 RA Assessment Tools Disease Activity Score (DAS28)

- Considers several factors to determine if symptoms are effectively managed.
- Number of joints in hands, wrists, elbows, shoulders, and knees that are swollen and/or tender.
- Visual Analog Score (VAS) global assessment
- ERS or CRP lab value

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40 RA Definition of Remission

- ACR/EULAR task force defines remission as a score of ≤ 1 on each of the following:
 - Tender Joint Count
 - Swollen Joint Count
 - C-reactive Protein Level (mg/dl)
 - Patient Global Assessment
- OR
- Simplified DAS of ≤ 3.3

Singh, J. A., Saag, K. G., Bridges, S. L., Aki, E. A., Bannuru, R. R., Sullivan, M. C., ... & Curtis, J. R. (2016). 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis & rheumatology*, 68(11), 1-26.

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41 RA Assessment Tools Disabilities of the Arm, Shoulder, and Hand Questionnaire (DASH)

- Assesses severity of functional limitation from impairment of the upper extremity in performing self-care activities of daily living, mobility, home maintenance, and recreation.
 - Responses scored 1-no difficulty to 5-unable
 - Optional work and music/sport sections
 - Higher score out of 100 reflective of greater level of disability

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42 RA Assessment Tools Five Times Sit to Stand Test (FTSS)

- Performance of repetitive sit to stand to assess lower extremity functional strength.
- Straight back chair with 16" seat height.
- Perform 5 sit to stand repetitions as quickly as possible keeping arms folded across chest.

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RA Smartphone Apps

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- Quality apps that include comprehensive tracking are lacking.
- Arthritis Power
 - Symptom tracking Function
 - Composite Measure of RA disease Activity
 - Lacking joint count function (swollen and tender)

Granger, R., Townsley, H., White, B., Langlotz, T., & Taylor, W. J. (2017). Apps for People With Rheumatoid Arthritis to Monitor Their Disease Activity: A Review of Apps for Best Practice and Quality. *JMIR mHealth and uHealth*, 5(2), e7. <http://doi.org/10.2196/mhealth.6956>

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RA Joint Protection and Energy Conservation

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- Application of proper ergonomics and biomechanics when performing ADLs protects joint from abnormal forces that may aggravate deformities, increase pain, and induce fatigue.

Joint Protection

- Distribute load on more than one joint
- Avoid positions favoring deformity
- Limit force when holding objects
- Use the stronger and larger joint to perform work

Energy Conservation

- Balance time with activity and rest
- Prioritize tasks, delegate
- Modify your environment

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RA Adaptive Equipment

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- Adaptive equipment for performance of activities of daily living (ADLs) promotes functional independence, energy conservation, and minimizes motions that foster joint subluxation.
 - Large door knobs or add handle levers
 - Flat press light switches
 - Ergonomic kitchen products
 - Use mugs instead of glasses

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RA Pharmacological Management

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- Non-opioid medications can provide relief of mild to moderate pain with opioids indicated for severe pain.
 - Non-opioid - Acetaminophen, Tramadol
 - Opioids – Fentanyl, Oxycodone, Hydromorphone
- Nonsteroidal Anti-inflammatory agents can inhibit the inflammatory process.
 - NSAIDs – Celebrex, Naproxen, Ibuprofen
- Corticosteroids slow radiographic progression and improve function through anti-inflammatory action.
 - Low-dose Prednisone

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RA Pharmacological Management Continued

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- Disease-Modifying Antirheumatic Drugs (DMARDs) disrupt the proinflammatory pathway through several mechanisms.
 - Methotrexate: Targets synovial adenosine receptors to inhibit the production of pro-inflammatory cytokines.
 - Adalimumab: Binds to TNF cytokine receptors inhibiting leukocyte migration.
- Biologics: Rituximab
 - Mediates B-cell apoptosis by targeting an antigen on the surface of lymphocytes.

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RA Pharmacologic Management Continued

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- Janus Kinase (JAK) Inhibitors target the protein inside the cells allowing influence on a wider range of hyperactive immune cells.
 - Tofacitinib – FDA approved
 - Baricitinib – clinical trials

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49 RA Antirheumatic Medication Monitoring

- Patients must be monitored for specific adverse reactions, toxicity, and side effects.
 - Opioid overuse – lethargy, mental confusion, respiratory depression, constricted pupils, pruritus, constipation
 - Opportunistic bacterial, viral, fungal infections
 - Hepatitis B reactivation
 - Tuberculosis
 - Shingles
 - Liver toxicity

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50 RA Research Advances

Current treatments are aimed at slowing down the tissue damage with new research to identify biologic targets for drug development.

- Genetics**
 - Gut microbiota
 - Gene specific treatments
- Disease Process**
 - TNF medication weaning
 - Tests for earlier diagnosis
- New Therapies**
 - Additional JAK Trials
 - Stem cell research
 - Smartphone and social media patient support tools

https://www.niams.nih.gov/Health_Info/Rheumatic_Disease/default.asp#ra_13 Copyright J. Gootkin 2019

51 Autologous Adipose Tissue Stromal Vascular Fraction (SVF) Cells

- SVF cells contain stem cells that possess regenerative and immunomodulatory properties.
- Harvesting SVF from an individual's fat and reintroducing the specific cells is theorized to
 - Target and attenuate joint inflammation
 - Enhance Treg production

<https://rheumatoidarthritisnews.com/2015/12/15/stemgenix-ra-clinical-study-stem-cell-therapy/>
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52 Systemic Lupus Erythematosus (SLE)

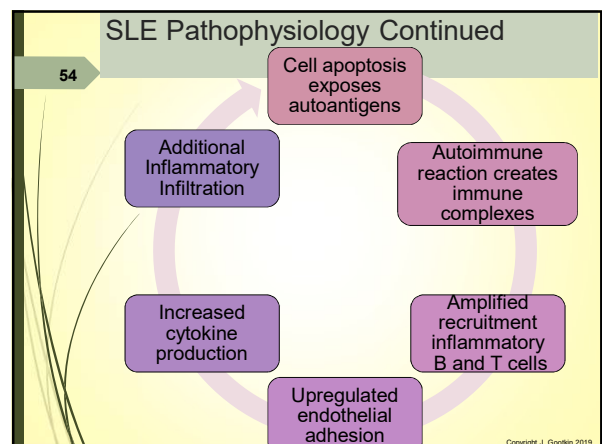
- Multisystem inflammatory condition with immune complexes that are damaging musculoskeletal, renal, hematopoietic, and central nervous systems.
- The condition is common of women of child bearing age with a significant female predisposition.
- Course of the disease is characterized by flares and remissions.

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53 SLE Pathophysiology

- The body recognizes specific intracellular nucleoproteins as antigens.
- During the immune reaction, these components are exposed on the dead and dying cells.
- Small immune complexes form that phagocytosis cannot clear so they are deposited on the endothelial lining of small blood vessels.
- The cycle of inflammation perpetuates creating a continuous supply of exposed nucleoproteins that initially triggered the response.

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SLE Pathophysiology Continued

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- The magnitude of the dysregulation of immunity in SLE suggests additional mechanisms that mimic a sustained antiviral response.
- A potential mediator may be Interferon Type 1 (INF1) which is a protein that binds to surface receptors on IFN- α that are produced by leukocytes.

Crow, M. K. (2014). Type I interferon in the pathogenesis of lupus. *The Journal of Immunology*, 192(12), 5459-5468.

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SLE Clinical Presentation

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- Polyarthralgia, polyarthritis, myalgia
- Oral ulcers
- Malar rash and discoid rash
- Photosensitivity
- Alopecia
- Peripheral and cranial neuropathy
- Renal pathology
- Pleurisy, pericardial effusion, pericarditis, peritonitis
- Fatigue, weight loss, fever
- Anemia

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SLE Diagnosis

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Clinical Criteria	Immunological Criteria
Acute Cutaneous Lupus	ANA
Chronic Cutaneous Lupus	Anti-dsDNA
Oral Ulcers	Anti-Sm
Non-scarring alopecia	Anti-Phospholipid
Synovitis \geq 2 joints	Low Complement C3, C4, CH50
Serositis - pleurisy	<ul style="list-style-type: none"> ■ At least 4 criteria (1 each category)
Renal Manifestations	
Neurological Manifestations	Or
Hemolytic anemia	<ul style="list-style-type: none"> ■ Biopsy proven nephritis and ANA or anti-dsDNA antibodies
Leucopenia/Lymphopenia	
Thrombocytopenia	

Systemic Lupus International Collaborating Clinics (SLICC) guidelines 2012
<https://resources.lupus.org/entry/revision-of-classification-criteria-for-systemic-lupus>

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SLE Vascular Complications

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- Lupus nephritis
- Antiphospholipid antibodies alter the body's anticoagulation ability resulting in clot formation.
 - Venothromboembolism
 - Transient Ischemic Attack (TIA)
 - Cerebrovascular Accident (CVA)
 - Myocardial Infarction (MI)
 - Pulmonary Embolism
 - Libman-Sacks Endocarditis
- Vascular spasm leads to livedo and Raynauds disease

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SLE Medical Management

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- "Treat to Target" strategy employed with goals of
 - Remission of organ manifestations
 - Prevention of early and late organ damage
 - Prevention of flares
- Exercise, diet, lifestyle modification to minimize multisystem complications
- Pharmacological Management

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SLE Rehabilitation Considerations

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- Monitor patient for systemic complications.
 - Thrombophlebitis
 - Nephritis
 - TIAs, angina
 - Seizures
- Patient education on limiting sun exposure.
- Close physician monitoring with pregnancy.

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61 SLE Rehabilitation Considerations Continued

- Distinguish headaches caused by lupus flare from those of other origin.
- Neuropsychiatric symptoms from altered CNS microvasculature leads to hemiparesis, spasticity, and other stroke-like symptoms.
 - Corticosteroids
 - Neurorehabilitation techniques

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62 SLE Assessment Tools SLE Disease Activity Index (SLEDAI-2k)

- Global score index to assess active disease considering manifestations in 9 organ systems with different point values awarded for each symptom:

Neurologic	Musculoskeletal	Renal
Vascular	Musculocutaneous	General
Respiratory	Hematopoietic	Cardiac

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63 SLE Assessment Tools SLE Responder Index (SRI-50)

- Utilizes symptoms identified on SLEDAI-2K with rating of change on next visit entered as a prorated value in recalculation.

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64 SLE and Exercise

- Goal is to manage fatigue and pain, increase cardiovascular fitness, and improve functional status.
 - Aerobic exercise
 - Muscle strengthening
 - Aquatic Therapy
 - Relaxation
 - Joint protection and energy conservation techniques

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65 SLE Patient Education

- Increase patient awareness of disease progression symptoms and self monitoring.
- Psychoeducational strategies have been shown to lower fatigue scores, improve physical function, and enhance mental health.
 - Patient and familial education
 - Social support
 - Self-efficacy and problem solving strategies

Karlson EW, Liang MH, Eaton H, Huang J, Fitzgerald L, Rogers MP, et al. A randomized clinical trial of a psychoeducational intervention to improve outcomes in systemic lupus erythematosus. Arthritis Rheum 2004;50:1832-41. Copyright J. Gootkin 2019

66 SLE Pharmacological Management

- NSAIDs and Corticosteroids to manage inflammation of cardiac, pleural, and synovial linings.
- Antimalarials are synthetic forms of quinine originally derived from tree bark.
 - Hydroxychloroquine
- Biologics block B-cell survival factors inducing apoptosis.
 - Rituximab
 - Belimumab
- Immunosuppressive agents
 - Azathioprine
 - Methotrexate
- Anti-thrombotic therapy

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SLE Research Advances

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- Intel Array Silicon Chip
 - Short pieces of the SLE associate protein are placed on silicon microchips which measure the multiple autoantibodies simultaneously.
- Treatment of Uncontrolled Lupus via Interferon Pathway (TULIP)
 - Phase III clinical trials are underway to block the Type 1 Interferon inflammatory pathway.
 - Anifrolumab
 - <http://med.stanford.edu/news/all-news/2012/08/stanfordintel-study-details-power-of-new-chip-to-diagnose-disease-analyze-protein-interactions.html>

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Type 1 Diabetes Mellitus (T1D)

68

Normal pancreatic function:

```

    graph LR
      Food --> Bloodstream
      Bloodstream --> Pancreas
      Pancreas --> Bloodstream
      Pancreas --> Insulin
      Insulin --> TargetTissues
  
```

- Typically diagnosed in childhood, the metabolic disorder is characterized by destruction of beta cells in the Islets of Langerhans of the pancreas leading to loss of insulin production and dysregulation of glucose.

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T1D Pathophysiology

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- Genetic mutation of certain variants of the HLA gene produces dysfunctional Tregs circulating in the body that fail to terminate the body's attack against its own beta cells.
- By failing to control the immune reaction, a chronic inflammatory response develops destroying the insulin producing cells of the pancreas.
- Without a sufficient level of functioning beta cells insulin production is not possible.

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T1D Controlling Glucose Levels

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- Insulin replacement is required for T1D with regular blood glucose monitoring through a home meter.
- The Target level varies for each individual with over 160 mg/dl considered high.

Time of Day	Person without DM	Person with DM
Before breakfast (fasting)	<100	70-130
Before lunch, dinner, snack	<110	70-130
Two hours after a meal	<140	<180
Bedtime	<120	90-150

Nathan, D. M., & for the DCCT/EDIC Research Group. (2014). The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview. *Diabetes Care*, 37(1), 9-16. <https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/GlucoseTestingDevices/default.htm>

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T1D Altered Insulin Levels

71

- Hypoglycemic or hyperglycemic episodes can occur if insulin is not appropriately monitored.
- Glucose level should be assessed prior to therapy sessions.

```

    graph TD
      Hypoglycemia --> Consequences
      Hyperglycemia --> Consequences
  
```

Hypoglycemia
Low blood glucose
Too much insulin
Seizures, coma, death

Hyperglycemia
High blood glucose
Insufficient insulin
Retinopathy, neuropathy, nephropathy

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T1D Hyperglycemia

72

- Insufficient insulin present for glucose to move into cells as energy with accumulation in bloodstream.
 - Too much food
 - Too little exercise
 - Skipped, insufficient, ineffective insulin
 - Stress, illness, infection, injury or surgery

```

    graph LR
      Liver[Liver releases glucose] --> Hyperglycemia[Hyper-glycemia]
      Hyperglycemia --> Ketoacidosis[Ketoacidosis]
      Ketoacidosis --> Coma[Coma and death]
  
```

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T1D Hyperglycemia Continued

73

- Symptoms
 - Fruity odor on breath
 - Nausea or vomiting
 - Xerostomia
 - Tachypnea and dyspnea
 - Polydipsia and polyuria
- Treatment
 - Exercise
 - If blood glucose 240 or higher, check urine for ketones and contact physician.
 - Determine if there is a pattern to the increased levels

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T1D Hypoglycemia

74

- Circulating glucose has been depleted by cells.
 - Ineffective delivery of insulin
 - Increased physical activity
 - Decreased food intake
 - Altered insulin sensitivity
 - Organic absorption problems
- Symptoms
 - Diaphoresis, lightheadedness, headache, fatigue, nervousness, unsteadiness, seizure
- Treatment
 - Consume glucose or simple carbs

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T1D Complications

75

Over time, circulating glucose damages the endothelial lining resulting in vascular complications.

Diabetic Retinopathy	• Vision assessment
Diabetic Nephropathy	• Glomerular Filtration Rate and Blood Urea Nitrogen monitoring
Diabetic Neuropathy	• Sensation and skin integrity assessment
Heart Disease and Stroke	• Blood pressure and cholesterol monitoring

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Thyroid Associations with T1D

76

- Autoimmune thyroid disease demonstrates greater incidence in individuals with T1D.
- Concurrent Celiac disease appears to increase this risk.

Weight gain Feeling cold Lethargy Dry skin Constipation Alopecia	Hashimoto's Disease Hypothyroidism	Diaphoresis Weight loss Restlessness Goiter Heat intolerance	Grave's Disease Hyperthyroidism
---	---------------------------------------	--	------------------------------------

Hughes, J. W., Riddlerworth, T. D., DiMeglio, L. A., Miller, K. M., Rickels, M. R., & McGill, J. B. (2016). Autoimmune diseases in children and adults with type 1 diabetes from the T1D exchange clinic registry. *The Journal of Clinical Endocrinology & Metabolism*, 10-2016Kurien, M., Mollazadegan, K., Sanders, D. S., & Ludvigsson, J. F. (2016). Celiac disease increases risk of thyroid disease in patients with type 1 diabetes: a nationwide cohort study. *Diabetes care*, 39(3), 371-375

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Inflammatory Bowel Disease (IBD) Associations with T1D

77

General term for disorders involving chronic inflammation of the gastrointestinal tract due to leukocyte infiltration.

```

graph LR
  IBD --> UC[Ulcerative Colitis]
  IBD --> CD[Crohn's Disease]
  UC --> UC_M[Restricted to mucosa]
  UC --> UC_C[Colon and rectum]
  CD --> CD_T[Transmural inflammation]
  CD --> CD_P[Patchy throughout GI tract]
  
```

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IBD Management

78

- Traditionally, systemic immunosuppressives and corticosteroids are utilized
- New medications specifically target integrins located on the surface of leukocytes to block their adhesion to endothelial cells.
 - Side effects – headache, nausea, nasopharyngitis

Singh, H., Grewal, N., Arora, E., Kumar, H., & Kakkar, A. K. (2016). Vedolizumab: A novel anti-integrin drug for treatment of inflammatory bowel disease. *Journal of Natural Science, Biology, and Medicine*, 7(1), 4-9. Khanna, R., Mosti, M. H., & Frazer, B. G. (2016). Anti-Integrins in Ulcerative Colitis and Crohn's Disease: What Is Their Place? *Cellular Diseases*, 34(1-2), 153-159.

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T1D Medical Management

79

- Management is multimodal with insulin replacement, laboratory monitoring, and lifestyle strategies.
- Insulin
- Glycosylated Hemoglobin A1C Monitoring
- Urine Monitoring For Ketones And Microalbuminuria
- Carbohydrate Controlled Diet
- Exercise
- Patient Education

<https://www.niddk.nih.gov/health-information/diabetes> Copyright J. Gootkin 2019

T1D History of Insulin

80

A timeline showing key milestones in the history of insulin treatment for Type 1 Diabetes Mellitus. The events are marked with colored circles and connected by a line that curves upwards from left to right, indicating the progression of time and medical advancement.

- 1910 Term "insulin" created
- 1915 Treatment calorie restriction
- 1921 Canine insulin injections successful
- 1923 Human commercial insulin injections produced
- 1949 Lock and Key action discovered
- 1955 Oral insulin available
- 1959 Two types of Diabetes formed

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T1D Insulin

81

- Insulin must mimic the normal way the pancreas would produce and distribute insulin.
 - Subcutaneous Delivery – syringe, pen, injector
 - Insulin Infusion Pump
- Calculation of the appropriate amount of insulin based on meal consumption of carbohydrates can be aided by technology.

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T1D Continuous Subcutaneous Insulin Infusion (CSII)

82

- A pump worn outside the body delivers continuous infusion of rapid acting insulin through a thin catheter in the skin.
 - The continuous glucose monitoring (CGM) device component takes frequent subcutaneous glucose measurements.
 - The patient preprograms the insulin amount and timing to account for carbohydrate intake with meals.

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T1D A1C Monitoring

83

- Glycosylated Hemoglobin A1C is a blood test measuring the amount of glucose that is attached to hemoglobin molecules in red blood cells providing information about the average blood glucose level over the past 2-3 months.
 - Target is below 7%
- A higher A1C level indicates elevated glucose levels that contribute to increased complications in other body systems.

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Food and Drug Administration Food Labeling

84

- Regulations for labeling of conventional foods and dietary supplements must provide updated nutrition information to assist consumers in maintaining healthy dietary practices.
- Compliance deadline varies based on annual sales of manufacturer.
 - Over \$10 million: July 2018
 - Under 10 million: July 2019
- Changes include removal of calories from fat, addition of "added sugars", Vitamin D and Potassium, and updated serving sizes.

<https://www.regulations.gov/document?D=FDA-2012-N-1210-0875> Copyright J. Gootkin 2019

85

Original Label

Nutrition Facts
Serving Size 2/3 cup (55g)
Servings Per Container About 8

Amount Per Serving		% Daily Value*	
Calories 230	Calories from Fat 72		
Total Fat 8g		12%	
Saturated Fat 1g		5%	
Trans Fat 0g			
Cholesterol 0mg		0%	
Sodium 160mg		7%	
Total Carbohydrate 37g		12%	
Dietary Fiber 4g		16%	
Sugars 1g			
Protein 3g			
Vitamin A		10%	
Vitamin C		8%	
Calcium		20%	
Iron		45%	

*Percent Daily Values are based on a diet of 2,000 calories. Your daily values may be higher or lower depending on your calorie needs.

	Calories	2,000	2,500
Total Fat	Less than	85g	80g
Sat Fat	Less than	35g	30g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate	Less than	300g	370g
Dietary Fiber		25g	30g

New Label

Nutrition Facts
8 servings per container
Serving size 2/3 cup (55g)

Amount per serving		% Daily Value*	
Calories 230			
Total Fat 8g		10%	
Saturated Fat 1g		5%	
Trans Fat 0g			
Cholesterol 0mg		0%	
Sodium 160mg		7%	
Total Carbohydrate 37g		13%	
Dietary Fiber 4g		14%	
Total Sugars 12g			
Includes 10g Added Sugars		20%	
Protein 3g			
Vitamin D 2mcg		10%	
Calcium 260mg		20%	
Iron 8mg		45%	
Potassium 235mg		6%	

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Labeling/Nutrition/ucm385663.htm#dates
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86

NEW LABEL / WHAT'S DIFFERENT

Servings: larger, bolder type

Calories: larger type

Updated daily values

Actual amounts declared

New footnote

Nutrition Facts
8 servings per container
Serving size 2/3 cup (55g)

Amount per serving		% Daily Value*	
Calories 230			
Total Fat 8g		10%	
Saturated Fat 1g		5%	
Trans Fat 0g			
Cholesterol 0mg		0%	
Sodium 160mg		7%	
Total Carbohydrate 37g		13%	
Dietary Fiber 4g		14%	
Total Sugars 12g			
Includes 10g Added Sugars		20%	
Protein 3g			
Vitamin D 2mcg		10%	
Calcium 260mg		20%	
Iron 8mg		45%	
Potassium 235mg		6%	

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

NEW: added sugars

Change in nutrients required

https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Labeling/Nutrition/ucm385663.htm#dates
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87

FOOD SERVING SIZES GET A REALITY CHECK

CURRENT SERVING SIZE

4 SERVINGS
1 PINT
200 CALORIES

NEW SERVING SIZE

3 SERVINGS
1 PINT
270 CALORIES

12 OUNCES
60 CALORIES

20 OUNCES
100 CALORIES

1 SERVING PER BOTTLE FOR EITHER BOTTLE SIZE

https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Labeling/Nutrition/ucm385663.htm#dates
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88

T1D Healthy Diet

- The 'plate method' helps limit the consumption of carbohydrates.

↑

Whole grains
Fruits
Non-starchy Vegetables
Healthy fat
Nonfat or low fat dairy
Proteins

↓

Added sugars
Starch vegetables
Butter, cream, shortening

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89

T1D and Exercise

- Regular exercise provides several benefits in the management of T1D in the pediatric and adult population.
 - Reduced and better maintained A1C levels
 - Decreased microalbuminuria
 - Improved cardiovascular disease risk profile
 - Decreased total daily insulin needs

Riddell, M. C., Gallen, I. W., Smart, C. E., Taplin, C. E., Adolphson, P., Lumb, A. N., ... & Annan, F. (2017). Exercise management in type 1 diabetes: a consensus statement. *The Lancet Diabetes & Endocrinology*. <http://www.smep.org.mx/wp-content/uploads/2017/04/Exercise-management-in-type-1-diabetes.pdf>
Copyright J. Gootkin 2019

90

T1D and Exercise Continued

- Adult exercise recommendation
 - 150 minutes accumulated physical activity per week
 - No more than 2 consecutive days without exercise
 - Resistance training 2-3 days a week
- Pediatric exercise recommendation is 60 minutes per day
- Exercise contraindications
 - Urine ketones ≥ 4.0 mmol/L
 - Recent hypoglycemia ≤ 50 mg/dL in 24 hours

https://www.smep.org.mx/wp-content/uploads/2017/04/Exercise-management-in-type-1-diabetes.pdf
Copyright J. Gootkin 2019

T1D Research Advances

91

Research is shifting away from immunosuppressive strategies toward understanding Treg function to develop interventions that protect or replace functional beta cell mass.

Immune Suppression	Immune Regulation
Medication to block T and B cell responses	Artificial Pancreas
	Antigen Based Therapy
	Interleuken Therapy
	Treg Cellular Therapy
	Islet Cell Transplantation

Consider This

Fulman, A. L., Brusko, T. M., Lee, M. R., Liu, W., Szot, G. L., Ghosh, T., ... Bluestone, J. A. (2009). Expansion of Human Regulatory T-Cells From Patients With Type 1 Diabetes. *Diabetes*, 58(3), 652-662. Copyright J. Gootkin 2019

T1D Artificial Pancreas

92

- The amount of insulin required throughout the day varies based on meals intake, physical activity, stress, and illness making stabilization of glucose levels challenging.
- An "artificial pancreas" is an externally worn device that can allow better stabilization of glucose levels when disturbances occur.
 - Glucose sensor
 - Control calculation system
 - Infusion pump

Boroux, D., Duun-Henriksen, A. K., Schmidt, S., Nergaard, K., Poulsen, N. K., Madsen, H., & Jørgensen, J. B. (2017). Adaptive control in an artificial pancreas for people with type 1 diabetes. *Control Engineering Practice*, 58, 332-342. Copyright J. Gootkin 2019

T1D Antigen Based Therapy

93

- Exploration has begun into preventing seroconversion to beta autoantibodies in babies.
- It is theorized that exposing neonatal oral mucosa to the antigen (insulin) will stimulate the immune response in a controlled manner guiding it toward self-tolerance.

Lamb MM, Simpson MD, Seifert J, Scott FW, Riewers M, Norris JM (2013) The association between IgG4 antibodies to dietary factors, islet autoimmunity and type 1 diabetes: The diabetes autoimmunity study in the young. *PLoS ONE* 8(2): e57936. Ziegler, A. G., Danne, T., Dunger, D. B., Berner, R., Puff, R., Kiess, W., ... & Bonifacio, E. (2016). Primary prevention of beta-cell autoimmunity and type 1 diabetes—The global platform for the prevention of autoimmune diabetes (GPPAD) perspectives. *Molecular Metabolism*, 5(4), 255-262. Copyright J. Gootkin 2019

T1D Interleukin Therapy

94

- The goal is to expand Tregs so that self-tolerance mechanisms are restored and some of the insulin producing beta cells are spared from damage.
- Administration of low doses Interleukin-2 (IL-2) appears to increase proliferation of Tregs that limit the destructive inflammatory response.
- Action of effector T-cells is preserved allowing beneficial immune responses to other pathogens to continue.

Dwyer, C. J., Ward, N. C., Pugliese, A., & Malek, T. R. (2016). Promoting immune regulation in type 1 diabetes using low-dose interleukin-2. *Current Diabetes Reports*, 16(6), 1-10. Copyright J. Gootkin 2019

T1D T-cell Therapy

95

- Treg Cellular Therapy:** Extracted Tregs from the individual's circulatory system or cryopreserved umbilical cord blood (UCB) can be isolated and expanded then reintroduced into the body to restore immune tolerance to the pancreatic beta cells.
- Engineered Tregs:** Designing Tregs with specialized receptors to recognize beta cells can protect them from the autoimmune attack and preserve overall immune system responsiveness.

<http://diabetes.ufl.edu/research/> Copyright J. Gootkin 2019

T1D Islet Cell Transplant

96

- Donor islet cells are removed using specialized enzymes for allo-transplantation
- A thin catheter in the upper abdomen infuses the cells into a portal vein of the liver.

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<https://www.niddk.nih.gov/health-information/diabetes/overview/insulin-medicines-treatments/pancreatic-islet-transplantation>

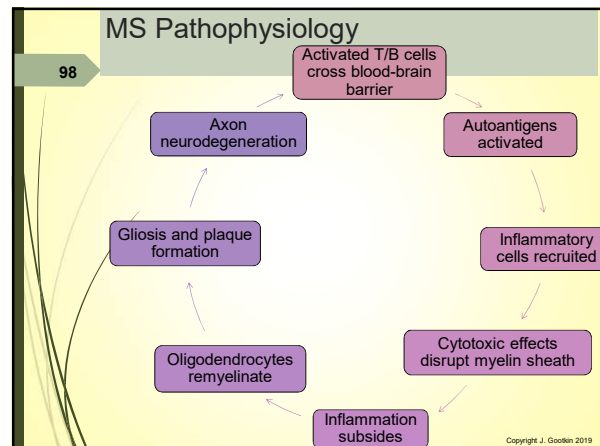
Multiple Sclerosis (MS)

97

- Neurodegenerative disease where immune neurotoxic inflammatory products in the central nervous system triggering an inflammatory response and neuronal stress resulting in demyelination.

Consider This

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MS Clinical Presentation

99

Clinically Isolated Syndrome (CIS)	• First episode of neurologic symptoms lasting at least 24 hours single neurologic symptom or multifocal
Relapsing-remitting (RRMS)	• Early active inflammation followed by remission with break through disease activity.
Secondary-progressive (SPMS)	• Begins as RRMS then becomes progressive with or without minor acute episodes
Primary-progressive (PPMS)	• Relentless disease progression
Progressive-relapsing (PRMS)	• Clearly progressive with acute exacerbations

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MS Clinical Presentation Continued

100

- Symptoms are extremely variable and diverse.
 - Sensory: paresthesias, dysesthesias
 - Lhermitte's sign
 - Visual: unilateral optic neuritis, diplopia
 - Motor: motor weakness, spasticity, dysphagia
 - Cerebellar: ataxia, dysmetria, dysidiadochokinesia, intention tremor, nystagmus, dysarthria, scanning speech
 - Pain, fatigue, cognitive impairment
 - Bowel, bladder, sexual dysfunction

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MS Medical Management

101

- Multimodal treatments focus on downregulation of the inflammatory process, up-regulation of the anti-inflammatory process, and management of symptoms:
 - Dietary modification
 - Omega-3 and Vitamin D supplements
 - Low sodium diet
 - Emotional wellness
 - Rehabilitation
 - Medication to manage disease process and exacerbations

Dunn, M., Bhargava, P., & Kalb, R. (2015). Your patients with multiple sclerosis have set wellness as a high priority--and the National Multiple Sclerosis Society is responding. *US Neurology*, 11, 80-6. Copyright J. Gootkin 2019

MS Rehabilitation Considerations

Emotional Considerations

102

- Pseudobulbar Affect (PBA) involves episodes of uncontrolled laughing and/or crying not related to their underlying mood.
 - Antidepressant medications
 - Educate patient on management strategies
- Adaptive coping and solution focused coping can enhance emotional well-being.

Dennison, L., Yardley, L., Devereux, A., & Moss-Morris, R. (2011). Experiences of adjusting to early stage Multiple Sclerosis. *Journal of health psychology*, 16(3), 478-488. Copyright J. Gootkin 2019

103 MS Rehabilitation Considerations Exacerbation

- Patient education should include strategies to minimize exacerbations.
 - Maintain good overall health status
 - Minimize stress
 - Major and minor stresses
 - Uthoff's symptom is an adverse reaction to heat that leads to a pseudoexacerbation.

External: Sun exposure, Humidity, Hot bath/pool, Air Temperature

Internal: Fever, Exercise

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104 MS Rehabilitation Considerations Fatigue

- Central fatigue is due to deterioration of the myelin sheath that slows neural conduction causing them to fatigue more quickly.
- Sensitivity to heat exacerbates fatigue
 - Submaximal exercise
 - Borg scale
- Energy conservation techniques
 - Adaptive equipment
 - Environmental modifications
- Maintain respiratory function
- Avoid extreme physical exertion

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105 MS Rehabilitation Considerations Sleep Disturbance

- Lesions to the hypothalamus, low melatonin levels, muscle cramps, and urinary urgency/frequency may contribute to difficulty staying and falling asleep.
- Promote good sleep hygiene and stimulus control
- Decrease daytime napping
- Sleep position modification and spasticity management
- Stress, anxiety, depression management

https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Documents/Sleep_Hughes_2016.pdf

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106 MS Assessment Tools Fatigue Severity Score (FSS)

- Self-report questionnaire measures fatigue severity and impact on activities and lifestyle.
- Items scored as 1 strongly disagree to 7 strongly agree
- Minimum score of 9 and maximum 63 with higher score indicating greater fatigue severity

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107 MS Assessment Tools Multiple Sclerosis Quality of Life-54 (MSQOL-54)

- Combines the Short Form 36 (SF-36) with 18 MS specific issues to generate physical health and mental health composite summary scores and allows subscales.

Cognitive function, Social function, Physical function, Health distress, Health perceptions, Role limitations emotional, Overall quality of life, Energy, Role limitations physical, Sexual function, Emotional well-being, Pain

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108 MS Assessment Tools Symptom Tracker App

- The National Multiple Sclerosis Society created the "Multiple Sclerosis Diagnosis and Management" smartphone app with information for clinicians and patients.
 - Diagnosis and management suggestions
 - Interactive assessment tools
 - MS Society resources
 - Symptom tracking tools

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MS Pharmacological Management

109

- Disease modifying medications can be biologics or immunosuppressives.
- Fingolimod: Binds to receptors that block lymphocytes from entering bloodstream from lymph nodes.
- Daclizumab: Bind to Interleuken-2 receptors mediating lymphocyte activation.
- Interferon beta-1a: Restores Tregs and enhances autoreactive T-cell apoptosis
- Corticosteroids

Costello, K and Halper, J. (2017) The use of disease-modifying therapies in multiple sclerosis: Principles and current evidence. A Consensus paper by the Multiple Sclerosis Coalition. Updated March 2017

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MS Medication Monitoring

110

- Patients should be monitored for side effects
 - Eye toxicity
 - Infections
 - Hepatic injury
- Smoking decreases medication effectiveness and increases risk of SPMS.

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MS Research Advances

111

- High Dose Immunosuppressive Therapy and Autologous Hematopoietic Cell Transplant (HDIT/HCT)
 - Immunosuppressive therapy followed by transplantation of a person's own blood-forming stem cells can induce sustained remission of relapsing-remitting MS.
 - Halted symptom progression
 - Relapse-free survival
 - Some improved mobility

Nash, R. A., Hutton, G. J., Racke, M. K., Popat, U., Devine, S. M., Steinmiller, K. C., ... & Stuve, O. (2017). High-dose immunosuppressive therapy and autologous HCT for relapsing-remitting MS. *Neurology*, 88(9), 842-852.

Copyright J. Gootkin 2019

MS Research Advances Continued

112

- A short diet mimicking fasting may induce immune responses to ameliorate demyelination.

Choi, I. Y., Piccio, L., Childress, P., Bollman, B., Ghosh, A., Brandhorst, S., ... & Wei, M. (2016). A Diet mimicking fasting promotes regeneration and reduces autoimmunity and multiple sclerosis symptoms. *Cell Reports*, 15(10), 2136-2146.

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MS Research Advances Continued

113

- Chronic Cerebrospinal Venous Insufficiency (CCSVI) proposes that insufficient blood drainage contributes to altered brain circulatory patterns and neuron degeneration.
- Restoring vascular flow through stent insertion may provide relief.

Hassoun, H. K., Al Essawi, R. W., Al Tirahhi, T., Al-Jussani, N., & Allebban, Z. (2017). Assessment of chronic cerebrospinal venous insufficiency among Iraqi multiple sclerosis patients by Echo color Doppler sonography.

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Autoimmune Disease Dietary Considerations

114

- Short-chain fatty acids (SCFA) that form when the body ferments soluble fiber promote strong bonds in the intestinal mucosa.
- These metabolites help prevent the "leaky gut" that contributes to autoimmune disease and promote Treg functioning.

Richards BL, Whittle SL, Buchbinder R. Neuromodulators for pain management in rheumatoid arthritis. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No.: CD008921.

Copyright J. Gootkin 2019

SCFA Food Sources

115	Resistant Starches	Barley, brown rice, beans, lentils, cooked and cooled potatoes, green bananas
	Inulin	Artichokes, onions, asparagus, leeks
	Arabinosyl	Cereal grains wheat bran, corn, rice, rye, oat, barley
	Pectin	Apples, apricots, carrots, oranges
	Butyrate	Parmesan cheese, goat milk, butter

Damen, B., Goetens, L., Broekaert, W. F., François, I., Lescaert, O., Trogh, I., ... & Verbeke, K. (2012). Consumption of breads containing in situ-produced arabinosyl oligosaccharides alters gastrointestinal effects in healthy volunteers. *The Journal of nutrition*, 142(3), 470-477. Copyright J. Gootkin 2019

- ### Mediterranean Diet
- 116
- The Mediterranean diet is associated with increased production of beneficial SCFAs.
 - High intake of whole grains, vegetables, fruits, legumes
 - Olive oil and fish instead of saturated fats
 - Low intake of red meat, poultry, dairy
 - Regular moderate ethanol
- Copyright J. Gootkin 2019

- ### Paleolithic Diet
- 117
- The Paleo diet mirrors dietary intake from the hunter-gatherer lifestyle.
 - 30-35% game meats and plant foods
 - Multiple daily servings of green, sulfur rich and intensely colored fruits and vegetables
 - High intake polyunsaturated fats
 - Limited processed foods, domesticated meats, dairy
- Copyright J. Gootkin 2019

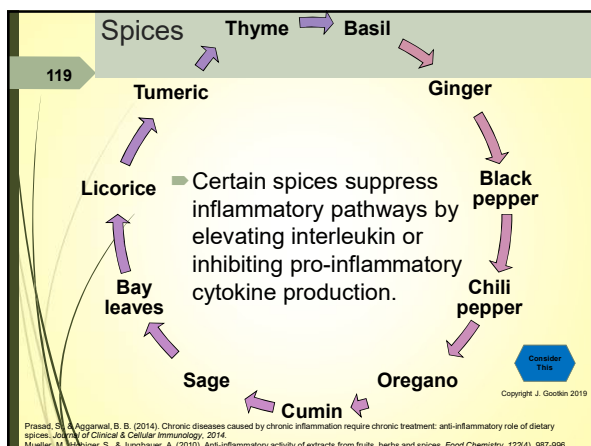
Anti-inflammatory Foods

118

- Avoiding foods that can trigger inflammation and increasing anti-inflammatory foods may aid in the management of autoimmune disease symptoms.

Omega-3 Fatty Acid — decreases inflammatory cytokines	Fruit, Vegetable, Whole Grain Fiber — decreases CRP levels	Extra virgin olive oil — blocks inflammatory enzymes
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- ### Nanotechnology
- 120
- Exploration has begun to develop a drug-delivery system that will introduce biodegradable nanoparticle-coupled Tregs into the body.
 - The “vaccine” will modulate the immune response by activating Tregs that will suppress the body’s attack of self-antigens.
 - The goal is to prevent the tissue destruction that leads to pathology development.
- http://technologylicensing.research.ufl.edu/technologies/13837_nanoparticl-e-coupled-regulatory-t-cells-for-the-treatment-of-type-1-diabetes
- Copyright J. Gootkin 2019

Conclusion

121

- Management of patients with autoimmune disease is multimodal including monitoring of to limit complications, provision of comprehensive care to enhance function, and ongoing research to develop treatments that accommodate for and prevent the self directed immune response.

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Clinical Trials and Medications

RxList Medication Search: Professional, Consumer, and Side Effects Sections
http://www.rxlist.com/drugs/alpha_a.htm

National Institutes of Health Clinical Trials
<https://www.nih.gov/health-information/nih-clinical-research-trials-you>

National Institute of Allergy and Infectious Disease: Information and Clinical Trials
<https://www.niaid.nih.gov/clinical-trials/find-a-clinical-trial>

National Institute of Arthritis, Musculoskeletal and Skin Diseases: Information and Clinical Trials
<https://www.niams.nih.gov/Research/default.asp>

Dietary Considerations

FDA Food Labeling: New Changes
<https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm385663.htm>

Type I Diabetes

FDA Diabetes: Treatment and Recall Information
<https://www.fda.gov/ForPatients/Illness/Diabetes/default.htm>

Lancet Exercise and Type 1 Diabetes Consensus Statement
<http://www.smep.org.mx/wp-content/uploads/2017/04/Exercise-management-in-type-1-diabetes.pdf>

Rheumatoid Arthritis

Centers for Disease Control and Prevention Arthritis Programs
Physical Activity <https://www.cdc.gov/arthritis/interventions/physical-activity.html#Recommended>

Arthritis Self-Management https://www.cdc.gov/arthritis/interventions/self_manage.htm

Funded State Arthritis Programs <https://www.cdc.gov/arthritis/partners/funded-states.htm>

Multiple Sclerosis

National Multiple Sclerosis Society: <https://www.nationalmssociety.org/Symptoms-Diagnosis/Newly-Diagnosed>

Multiple Sclerosis Diagnosis and Management App
Apple <https://itunes.apple.com/us/app/multiple-sclerosis-diagnosis/id480116542?mt=8>
Android https://play.google.com/store/apps/details?id=com.bbi.national_multiple_sclerosis_society&feature=search_result#?t=W251bGwsMSwXLDEsImNvbS5iYmkubmF0aW9uYWxfbXVsdGlwbGVfc2NsZXJvc2l2X3NvY2lldHkiXQ

Assessment Tools

Disease Activity Score (DAS28) <http://www.nras.org.uk/healthcare-professionals>

Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH)
<http://dash.iwh.on.ca/about-dash>

SLE Disease Activity Index (SLEDAI-2k) online version
<http://tools.farmacologiaclinica.info/index.php?sid=10052>

Fatigue Severity Scale (FSS)
<https://www.saintalphonsus.org/documents/boise/sleep-Fatigue-Severity-Scale.pdf>

Multiple Sclerosis Quality of Life-54 (MSQOL-54)
[https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-54-\(MSQOL-54\)](https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-Researchers/Clinical-Study-Measures/Multiple-Sclerosis-Quality-of-Life-54-(MSQOL-54))