NMDD312

Session 10: Immune System Disease
Part I
Session Overview

- Immune system disease (part 1) *Autoimmune diseases*
- Dietary therapeutics & interventions in autoimmune disease
- Autoimmune Diseases:
  - Multiple sclerosis - Screening and assessment
  - Myasthenia gravis - Screening and assessment
  - SLE - Screening and assessment
  - Rheumatoid arthritis - Screening and assessment
  - Scleroderma - Screening and assessment
  - Sarcoidosis - Screening and assessment
Therapeutic Considerations
Autoimmunity

*Multifactorial shift of immunity to reduced tolerance of self. Combining genetic, environmental, hormonal and immune factors.*

Environmental factors implicated include:
- Viral and bacterial infections triggering CD4 cells and raised inflammatory markers
- Chemical and/or drug exposure
- Dietary antigens (e.g. coeliac disease)
- Stress

(Janeway et.al. 2001; Fujinami et.al, 2006; Sarris & Wardle, 2010, p. 538-540)
Dietary & Nutritional Prescription

Autoimmunity

**Vitamin D**
- Generates appropriate T and B lymphocyte responses to activation including down-regulating inappropriate autoantibody production.
- Modulates dendritic cell responses (regulates responses to self) and macrophage responses (regulating release of inflammatory cytokines and chemokines).
  (Arnson et al, 2007; Marquez et al. 2010)

**Omega 3**
- Increasing the omega 3 composition of immune cells can alter the function of phagocytes, T-cell signalling and modulates the immune effects with antigen presentation.
- Suppresses the production of PGE2 (pro-inflammatory).
  (Calder, 2007)
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Autoimmunity

**Zinc**
- Modulates apoptosis which plays key roles in immune integrity via the elimination of anti-self and nonsense clones (protects against gene mutation) and the successful killing of aberrant target cells by cytolytic T cells.

(Fraker et.al. 2000, p. 1403s)

**Vitamin B12**
- Deficiency presents with raised and sustained levels of TNF-α and greater susceptibility to auto-reactivity

(Richardson, 2002)
Dietary & Nutritional Prescription

Autoimmunity

**Probiotics** *Bifido. bifidum & Bifido. Breve*
- Enhance antibody responses & stimulate IgA
  
  *(Isolauri et.al. 2001)*

**Vitamin C**
- Facilitates & regulates immune function including:
  - Increasing levels of macrophage activity
  - Lymphocyte & antibodies (IgA, IgG, IgM) production
  - Modulates prostaglandin synthesis

  *(Schlenker & Long, 2007).*
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Autoimmunity

**Arginine**
- Is required in greater quantities of periods of growth, illness or injury
- Found to increase T-cell immune responses
- Supports healthy collagen formation

**Glutamine**
- Utilised by rapidly dividing cells as an energy source.
- Integral component of the antioxidant system and liver detoxification processes

(Payne & Barker, 2010, p. 120)
Multiple Sclerosis
Multiple Sclerosis

- Characterised by destruction of the myelin sheath and the formation of scar tissue.
- Destruction leads to the distortion or interruption of nerve impulses.

**Symptoms**

- Numbness and/or tingling in the limbs
- Loss of coordination
- Weakness
- Paralysis
- Loss of vision

(Nelms, et. al 2007)
Types of Multiple Sclerosis

- Relapsing-remitting (RR) MS
- Primary-progressive (PP) MS
- Secondary-progressive (SP) MS
- Progressive-relapsing (PR) MS

Source: Medinet
MS Australia

- Drugs used in Australia
Therapeutic Considerations

Multiple Sclerosis

- The most common form of MS is *relapsing-remitting* MS
  - Characterised by alternating periods of exacerbation and remission of symptoms without progressive worsening of symptoms.

- Approximately half of individuals diagnosed with relapsing-remitting MS progress to *secondary-progressive* MS within 10 years
  - The severity of symptoms begin to progressively worsen.

(Nelms, et. al, 2007)
Therapeutic Considerations
Multiple Sclerosis

**Drug Related Nutritional Implications**

- High-dose steroids: deplete vitamin B12 and folate
  
  (Mahan & Escott-Stump, 2009, p. 1093)

- Centrally acting skeletal muscle relaxants
  
  - Phenylalanine and high protein meals block the absorption of these drugs.
  - Take drug 2 hours before or 4 hours after to maintain bioavailability
  - Vitamin B3 has been found to stimulate GABA receptors without binding, thereby having an additive effect.

  (Stargrove et al. 2008)

- Glutamine and Vitamin B6 also potential for a therapeutic additive effect

  (Braun & Cohen, 2010)
Therapeutic Considerations
Multiple Sclerosis

**Dysphagia**

- When dysphagia presents the use of texture modified diets should be included.
- Diets should move from solids to mashed or pureed foods and thickened liquids to minimise the potential for aspiration

(Mahan & Escott-Stump, 2009, p. 1094)
Therapeutic Considerations
Multiple Sclerosis

**Bladder Issues**

- Neurogenic bladder issues can present.
  - This is implicated in urgency, frequency and incontinence at night.
  - Fluids should be distributed throughout the day and limited towards bedtime.
- UTI’s are common.
- Use of unsweetened cranberry juice may be beneficial.
  
  (Mahan & Escott-Stump, 2009, p. 1094)
Therapeutic Considerations
Multiple Sclerosis

**Constipation & Diarrhoea**

- Constipation is reported in a third of MS sufferers due to muscle weakness, immobility and low fibre intake.
- Both common and there is increased incidence of fecal impaction.
- High fibre, adequate fluid & prunes
  (Mahan & Escott-Stump, 2009, p. 1094)
- *Lactobacillus plantarum* has been found to aid constipation and moderate T-cell activity in Multiple Sclerosis
  (Kidd, 2005)
Dietary & Nutritional Prescription
Multiple Sclerosis

**Saturated Fatty Acids**
- Diets high in SFA’s are implicated as a risk factor for MS presentation.
- Inclusion of PUFA’s and omega 3 fatty acids is well warranted. (Katz, 2008, p. 262; Moore, 2010, p. 492)
- Omega 3 fatty acids suppress the inflammatory response by enhancing PGE-3 presentation and down regulating PGE-2 production. (Kidd, 2005; Osiecki, 2006)
Dietary & Nutritional Prescription
Multiple Sclerosis

**Antioxidants**

- Oxidative stress has been speculated to play a role in the development of MS.
- Diets rich in antioxidants, combined with supplementation of vitamins C, E and selenium are indicated. (Moore, 2010, p. 492)
- Vitamin E has been found to down-regulate PGE-2 activity (Kidd, 2005; Osiecki, 2006)
Dietary & Nutritional Prescription
Multiple Sclerosis

Vitamin B12

- Decreased levels of vitamin B12 commonly present in MS patients.
- The symptoms of vitamin B12 deficiency and MS are markedly similar

Factors involved in reduced vitamin B12 deficiency include:
- Inadequate intake (vegetarian)
- Reduced HCl levels and intrinsic factor
- Terminal ileum conditions (Crohn’s disease)
- Intestinal worms

(Miller et al. 2005)
Dietary & Nutritional Prescription

Multiple Sclerosis

*Testing for Vitamin $B_{12}$ deficiency*

- Common test is serum $B_{12}$ levels - very inaccurate
- Methylmalonic acid and homocysteine levels is much more accurate
  - May be affected by folic acid levels

(Miller et.al. 2005)
Dietary & Nutritional Prescription
Multiple Sclerosis

**Vitamin D**

- Vitamin D deficiency is implicated in alterations to T cell function and the presentation of this auto-immune condition.
- Increases have been found to suppress auto-immunity and regulate suppressor T-cell activity
  
  (Kidd, 2005; Osiecki, 2006)
- Prevalence increases the further away an individual resides from the equator thereby having limited sun exposure.

Dietary & Nutritional Prescription
Multiple Sclerosis

**Swank Diet**
- Swank diet (very low saturated fat intake [<15g/day]) supplemented with vegetables and cod liver oil has been used for MS.

(Moore, 2010, p. 492)

**Jelinek Diet**
- [http://www.overcomingmultiplesclerosis.org/](http://www.overcomingmultiplesclerosis.org/)
Dietary & Nutritional Prescription
Multiple Sclerosis

Calcium

- In MS, there is reduced activity within the body for bone maintenance and muscle/neuronal firing.
- Combined with vitamin D, results in stabilisation of lymphocyte activity and increased IL-4 and TGF-b1 activity
  
  (Kidd, 2005; Osiecki, 2006)

- Osteoporosis is common in MS patients.
- Diet requires adequate calcium and vitamin D.
  
  (Moore, 2010, p. 492)
Myasthenia Gravis
Myasthenia Gravis

From *Immunity: The Immune Response in Infectious and Inflammatory Disease* by DeFranco, Locksley and Robertson

- Normal
- Muscle
  - \( \text{Na}^+ \)
  - \( \text{Na}^+ \)
  - \( \text{Na}^+ \)
  - \( \text{ACh} \)

- Myasthenia gravis
  - No muscle contraction
  - Endosome
Therapeutic Considerations
Myasthenia Gravis

Individuals fatigue easily while eating so the following should be observed:

- Nutritionally dense foods at the beginning of the meal is easier to chew before the individual tires.
- Small, frequent meals.
- Limit physical activity before meals.
- Fatigue while eating can increase the chances of food aspiration.

(Schlenker & Long, 2007; Mahan & Escott-Stump, 2008)
Therapeutic Considerations
Myasthenia Gravis

Drug Induced Nutritional Considerations
Immunosuppressant Drugs (*incl. systemic Corticosteroids*)

- Impair zinc & calcium absorption & affect calcium & vitamin D metabolism.
- Increased excretion of chromium.
- Reduced serum levels of vitamin B12, folate and vitamin B3
- Require the concurrent usage of potassium

(Mahan & Escott-Stump, 2008; Stargrove et.al 2008)
Dietary & Nutritional Prescription
Myasthenia Gravis

**Acetylcholine**
- Phosphatidylcholine is an acetylcholine substrate. (Farber et al. 2000)
- Vitamin B1, B5, B6, B12 and folate are required as cofactors in ACh synthesis (Malouf & Evans, 2008)
- Acetyl-L-carnitine has been found to enhance the action of ACh (Spagnoli et al. 1991)
- Inositol is a secondary messenger for cholinergic receptors (Huang et al. 2001)
Systemic Lupus Erythematosus
Systemic Lupus Erythematosus

A systemic disease with immunologic mechanisms of tissue injury.

Etiology implications include:

- Viral infection (*Epstein-Barr*) altering immune responses in predisposed individuals.
- Heredity & genetic components (HLA A1, HLAB8, HLADR3).
- Female based condition (70-90%) (Hajj-ali, 2008)
- UV light has been found to trigger SLE flares.
- There is a form of drug induced (reversible) SLE. (Kumar & Clark, 2007)
Therapeutic Considerations
Systemic Lupus Erythematosus

**Drug Induced Nutritional Implications**

*Anti-malarial drugs*
- Vitamin E reduces bioavailability of the drug
- Depletes folate

*NSAID’s*
- Concurrent usage of vitamin E, omega 3, ginger & turmeric can reduce pain more effectively.
- Garlic, quercetin & SAMe are hepatoprotective (paracetamol)
- Deplete vitamin C (aspirin)

(Braun & Cohen, 2010; Sarris & Wardle, 2010)
Anti-inflammatory Nutrients

- SLE presents with the over-expression of pro-inflammatory cytokines IL-17, IFN-y203 (linked to B-cell activation and auto-antibody responses)
  
  (Sarris & Wardle, 2010, p.555)

- Anti-inflammatory nutrients (*vitamin E, vitamin C*), omega-3 fish oil and phytochemicals (*bioflavonoids, volatile oil components*) have been found to inhibit pro-inflammatory prostaglandin and cytokine levels.
  
  (Osiecki, 2006; Schlenker & Long, 2007; Wright, et al. 2008; Sarris & Wardle, 2010)
Dietary & Nutritional Prescription
Systemic Lupus Erythematosus

**Vitamin B12**

- DNA requires methylation. Deficiency of vitamin B12 in this process is implicated in CD4+ induced auto-reactivity (experimental models present with lupus-like disease in animal tests)
- UV light inhibits DNA methylation which in turn triggers lupus flares

(Richardson, 2002)
Dietary & Nutritional Prescription
Systemic Lupus Erythematosus

**Indole-3-Carbinole (I-3-C)**
- Oestrogens promote disease activity (female predominant in reproductive age)
- I-3-C alters the metabolite output from the liver (2(OH)oestrogen predominant over 16a(OH)oestrogen (more biologically active) which has modulated disease responses
  (McAlidon et.al. 2001)

**Diindolylmethane (DIM)**
- DIM increases oestrogen C-2 hydroxylation.
  (Sepkovic, et.al. 2009)
Dietary & Nutritional Prescription
Systemic Lupus Erythematosus

**Vitamin D**

- Deficiency commonly presents in active SLE cases with concurrent changes in bone remodelling related to disease activity.
- Raised cytokine levels are also commonly present.

(Borba et al, 2008)
Therapeutic Considerations
Systemic Lupus Erythematosus

Drug Induced Nutritional Implications

Systemic Corticosteroids
- Deplete calcium, chromium, potassium, zinc, folate, vitamin B3 & B12.

(Harkness & Bratman, 2003; Mahan & Escott-Stump, 2008; Stargrove et.al 2008)

Cyto-toxic Immuno-suppressants (Methotrexate)
- Depletes folate.
- Concurrent usage of folate, glutamine, vitamin A, C, E and zinc diminish drug-induced side effects.

(Ortiz et.al. 2000; Bryant & Knights, 2010; Sarris & Wardle)
Rheumatoid Arthritis
Rheumatoid Arthritis

Inflammatory disease that presents with antibodies to articular cartilage and damage to sub-chondral bone. (Kumar & Clark, 2009)
Therapeutic Considerations
Rheumatoid Arthritis

Serum testing can include:
- Rheumatoid factor (T cell production)
- Anti-CCP antibodies
- Inflammatory cytokines
- Activated mast cells (histamine & TNF-α)

Other tests include:
- X-rays and MRI scans of affected joints
- Joint aspiration

(Kumar & Clark, 2009)
Therapeutic Considerations
Rheumatoid Arthritis

**Dietary Patterns**

- Link between dietary pattern and immune function (antioxidants, micronutrients, zinc and fatty acids)
- Vegetarian diet has seen a reduction in RA symptoms when combined with omega3.
  - Levels of C-RP, IL-6 and TNF-α were significantly reduced
  - Fasting followed by vegetarian diet improves symptoms
- Vegan/vegetarian diets are associated with changes in the bowel flora presentation and improvement in disease symptomatology (possible gut dysbiosis)
  
  (Katz, 2008, p. 251; Rayman & Pattison, 2008)
Therapeutic Considerations
Rheumatoid Arthritis

**Excess Body Weight**
- Increases joint stress $\rightarrow$ increased risk of CVD due to inactivity

(Katz, 2008, p. 251; Rayman & Pattison, 2008)

**Reduced Body Weight**
- Rheumatoid cachexia (15%) is characterised by increased catabolism and REE, muscle wasting and anorexia, and is associated with the production of the pro-inflammatory cytokines that play a key role in inflammation-mediated loss of appetite, weight loss and joint destruction.

(Rayman & Pattison, 2008)
Therapeutic Considerations
Rheumatoid Arthritis

Drug Induced Nutritional Implications

- Drug therapy is implicated in causing anorexia or nausea and down-regulating the appetite
  
  (Katz, 2008, p. 254)

Penicillamine

- Binds to metals reducing bioavailability and increasing excretion (Copper, Iron, Magnesium & Zinc) & antagonises vitamin B6.

  (Stargrove et al. 2008)
Dietary & Nutritional Prescription
Rheumatoid Arthritis

Nutritional Deficiencies

- RA patients commonly present with reduced intakes or deficiencies in calcium, folic acid, vitamin E, zinc, selenium, vitamin B6 & vitamin B12.
  
  (Mahan & Escott-Stump, 2008, p. 1055)

- Iron deficiency is common due to NSAID-induced GIT bleeding. Iron in high doses exacerbates the presentation of free radicals in joints when micro-trauma presents.

- Copper aids the crosslinking of collagen and elastin to sustain connective tissue strength.

  (Rayman & Pattison, 2008)
Dietary & Nutritional Prescription
Rheumatoid Arthritis

**Nutritional Deficiencies**

- Calcium and vitamin D malabsorption are common in the advanced stages of RA.  
  (Mahan & Escott-Stump, 2008, p. 1055)
- Vitamin D deficiency commonly presents in RA.
- Possible implication with greater risk of immune system producing self-reactive Th1 cells and autoimmunity.  
  (Rayman & Pattison, 2008; Leventis and Patel, 2008)
Food Intolerance

- Implicated as a sustaining factor in the presence of symptoms rather than a primary cause.
- Foods implicated include:
  - Gluten
  - Cereal grains
  - Lectins
  - Spices
  - Strong coffee
  - Alcohol

(Rayman & Pattison, 2008; Katz, 2008, p. 254)
Dietary & Nutritional Prescription
Rheumatoid Arthritis

*Omega 3*

**Dosage**
- 12gm/day of linoleic acid (can be more in some cases)
- 4gm/day $\alpha$-linolenic acid
- Restricting arachidonic acid to less than 50mg/day

- Reduces the number of tender joints and an overall reduction in the requirements of NSAIDs in those suffering with RA.

(Katz, 2008, p. 253)

- Balancing the ratio of omega 6: omega 3 in RA patients that were otherwise low in omega 3 significantly reduced symptoms and overall health scores

(Rayman & Pattison, 2008)
Dietary & Nutritional Prescription
Rheumatoid Arthritis

**Antioxidants**

- Free radicals and pro-inflammatory cytokines (TNF-α) have been found to contribute to joint inflammation and damage in RA (Bae et al. 2003)
- Combination of antioxidant nutrients – vitamin E, vitamin C & selenium confer some benefit (Katz, 2008, p. 253)
- Deficiencies of serum antioxidant levels (vitamin E, C, β-carotene, Selenium & Zinc) commonly present as deficient (Cerhan et al. 2003; Rayman & Pattison, 2008)
Scleroderma
Scleroderma

- Means ‘hard skin’.
- Group of autoimmune diseases that present with the deposition of fibrous connective tissue in and around the skin and internal organs.
- Can affect the blood vessels and joints
- Free radical and oxidative damage further exacerbates the disease presentation

(Mahan & Escott-Stump, 2008, p. 1042)
Therapeutic Considerations
Scleroderma

- Dysphagia presents due to thickening of the throat.
  - The implementation of a thickened food and liquid diet may be warranted
- Malabsorption of lactose, vitamins, fatty acids, and minerals commonly presents.
- High-energy protein may correct or prevent weight loss (common presentation).
- Dry mouth and tightening facial skin can make eating difficult.
- Requires adequate fluid intake.

(Mahan & Escott-Stump, 2008, p. 1044, 1059)
Dietary & Nutritional Prescription

Scleroderma

- Moist foods (makes it easier to swallow)
- If GORD presents – food modification, small frequent meals
- Avoiding late-night eating
- Reduction in alcohol, caffeine, spicy fatty foods

(Mahan & Escott-Stump, 2008, p. 1044, 1059)
Dietary & Nutritional Prescription

Scleroderma

Para-aminobenzoic acid (PABA)
- Anti-fibrotic action that has been found to soften and thin the skin (12gm /day).

Vitamin E
- Significant oxidative stress presents in scleroderma.
- Vitamin E is used to stabilise lysosomal membranes & also due to the anti-fibrinolytic action.

(Gaby, 2006, p. 189)
Dietary & Nutritional Prescription
Scleroderma

Vitamin D
- Doses of 10,000 to 12,500IU/day for three months have been found to reduce scleroderma symptoms.

S-Adenosylmethionine (SAMe)
- Supplementation presented with significant skin improvements. Other areas of the disease did not respond.

Bromelain
- Supplementation of 160-180mg/day have been found to improve hand movements and swallowing function

(Gaby, 2006, p. 191-192)
Dietary & Nutritional Prescription

Scleroderma

**Zinc**
- Deficiency within the erythrocytes, platelets and granulocytes commonly presents in scleroderma patients.
- Penicillamine, commonly prescribed to treat scleroderma has been found to increase zinc excretion
  
  (Gaby, 2006, p. 192)
Sarcoidosis
Sarcoidosis

- Systemic inflammatory disease that presents as a Th1 immune dysfunction.
- Abnormal nodules appear all over the body, but the lymph nodes and the lungs are affected in 90% of cases.
- Genetically susceptible alleles on the same gene as multiple sclerosis and systemic lupus erythematosus.
- Chronic inflammatory disease that presents with high levels of reactive oxygen species (ROS)

(Boots et al. 2011, p506)
Therapeutic Considerations

Sarcoidosis

Typical symptoms may include:

- Cough
- Fever
- Chest pain or discomfort
- Shortness of breath
- Tiredness and lethargy
- Facial swelling
- Arthritis, particularly of the large joints
- Painful red lumps called *erythema nodosum* on the front of the legs
Dietary & Nutritional Prescription

Sarcoidosis

**Quercetin**

- Low levels are implicated in the inflammation that can trigger sarcoidosis.
- Quercetin is the most active ROS scavenger – more potent than glutathione and vitamin E
- Potent anti-inflammatory reducing TNFα and IL-8 (both raised in sarcoidosis)

(Boots et al. 2011, p506)
Dietary & Nutritional Prescription
Sarcoidosis

**Vitamin D**

- Almost always consistently elevated in sarcoidosis.
- Severity of the systemic inflammation was roughly proportional to the amount of 1,25-D that presented in assay (Marshall & Marshall, 2003, p. 298)
- 25(OH)D3 is insufficient but the 1,25(OH)2D3 are raised (Sage, Sudbaker, Burke & Lim, 2011, p.796)
References


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Tutorial 10:

Immune System Disease Part I
Dietary Intervention in Immune System Disease

Students form small tutorial groups to review 1 of the following papers


Dietary Intervention in Immune System Disease

As you read the paper, highlight the key points that the author/s make about the dietary intervention and the presentation of RA.

- What can you take from these publications?
- How would this influence how you would treat a client who presents with RA?
- Is there anything about the paper/study design that you don’t agree with?
  - Justify your response.
Dietary Intervention in Immune System Disease

- What would be your top 5 dietary recommendations to a client who presented with RA?
  - What advice would you give them to make these recommendations practical?
  - What could be possible compliance issues with these clients?
Dietary Intervention in Immune System Disease

Groups present their findings to the class for feedback and further discussion.