NMDC221 Session 23: Integumentary System Disease Part I
Topic Summary

Integumentary System Disease: Part II
Nutritional management of specific immune conditions with consideration of drug-nutrient interactions

- Psoriasis
- Acne vulgaris
- Acne rosacea
Psoriasis
Psoriasis

A common chronic, recurrent disease characterised by:

- Dry, well-circumscribed, silvery, scaling papules & plaques of various sizes and severity (1-2 lesions to widespread dermatosis)
- Sometimes associated with disabling arthritis
- 2-3% of the population
- Genetic predisposition
  (Davidson & Haslett, 2002, p. 900)

http://www.dermatology.co.uk/media/images/PSORIASIS_DRY_ON_ARM.jpg
Psoriasis

- Around 30 per cent of people affected by psoriasis will be able to identify relatives who have or have had psoriasis.

- **Types of skin psoriasis**
  - Plaque psoriasis – the most common form
  - Pustular psoriasis – a more severe form of psoriasis that can be painful
  - Guttate psoriasis – found mostly in children
  - Napkin psoriasis – characteristically seen in infants between two and eight months of age
  - Flexural psoriasis – affects body folds and genital areas
  - Erythrodermic psoriasis – a severe form requiring hospitalisation.
Psoriasis

- The areas that are most commonly affected are the scalp, elbows and knees, but skin psoriasis can occur anywhere on the body.

- Psoriasis is defined by a series of linked cellular changes in the skin:
  - Hyperplasia of epidermal keratinocytes,
  - Vascular hyperplasia and ectasia,
  - and infiltration of T lymphocytes, neutrophils, and other types of leucocyte in affected skin (Krueger and Bowcock, 2005)
Psoriasis

Factors Implicated in Provoking or Aggravating Psoriasis:

- Infections: Bacteria (Strep, Staph), Fungi (Malassezia, Candida albicans), Viruses (papillomaviruses, retroviruses)
- Medication: lithium, β-blockers, antimalarial agents, NSAID’s and angiotensin-converting enzyme inhibitors.
- Smoking
  (Ropirin & Tencomnao 2010)
- Stress & mood disorders has been found to create inflammatory and immune reactions
  (Davidson & Haslett 2002; Brown et al, 2004)
Psoriasis

Factors Implicated in Provoking or Aggravating Psoriasis:

- GIT: Dysbiosis and altered gut permeability allows access of dietary or microbial antigens to GIT and systemic immune system
  - This may stimulate non-specific immune response & produce local or systemic inflammation
  - Microbial antigens may cross react with self-antigens and stimulate autoimmunity (*molecular mimicry*).

(Galland, 2009; Steel 2010)
Psoriasis

Factors Implicated in Provoking or Aggravating Psoriasis:

- Diet: May play a role in the aetiology and pathogenesis of psoriasis
  - Various dietary factors showing beneficial effects as anti-inflammatory and antioxidant properties
  - Elevated gluten sensitivity is common. Gluten sensitivity causes systemic inflammatory responses
    (Wolters 2004; Traub 2007; Galland 2008)
  - Serotonin has been considered as one of the mediators of pruritus in psoriasis
    (Wolters 2004; Ropirin & Tencomnao 2010)
Psoriasis

Nutritional Treatment

Antioxidants

- Oxidative stress and increased free radical generation have been linked to skin inflammation and psoriasis
- Adequate levels of antioxidant vitamins and minerals therefore are required (Wolters 2004)

Fish Oils

- Abnormal levels of leukotrienes are involved in the development and progression of psoriasis.
- Eicosapentaenoic acid (EPA) counters this with anti-inflammatory effects
Psoriasis

Nutritional Treatment

- Severe psoriasis has been associated with nutritional deficiencies due to accelerated loss of nutrients from hyperproliferation and desquamation of the skin’s epidermal layer (Wolters, 2010)

- Individual patient assessment necessary to determine level of sensitivity to dietary components and depletion of nutrients
Psoriasis

Immune System

- Immunosuppressive drug therapy (cyclosporine) reduces lesion presentation suggesting an immunologic cause (Davidson & Haslett, 2002)
Psoriasis

Clinical Investigations:
- Biopsy
- CRP

Treatment Aims
The autoimmune and inflammatory link in psoriasis requires a systematic treatment approach
- Reducing activity of the cells
- Reducing systemic inflammation
- Minimizing discomfort and embarrassment
- Consider precursors to serotonin
Psoriasis

Topical Management

- Oatmeal baths may reduce itching
- Bath oils/ soap substitutes
- Emollients – changes in skin moisture reduces the barrier function and allowing triggers and allergens to penetrate the skin. Dry skin can increase itching which in turn creates physical damage. Can potentially reduce the requirement for corticosteroids
- Emollients can be used as soap alternatives.
- Occlusive treatment can be used if the site is wet, exuding or inflamed.

UV light therapy - dermatologist (Bennett, 1999)
Acne Vulgaris
Acne Vulgaris

Acne Presents with Increased:

- Testosterone & 5-alpha reductase production (testosterone → dihydrotestosterone DHT) = excess sebum and keratin production of skin pore

- Overgrowth of *Propionibacterium acnes* (Osiecki, 2006)
Acne Vulgaris

Blockage of canals

- Incomplete → blackheads (no inflammation)
- Complete → whiteheads (inflammation)
- Rupture of hair canal → cysts and pustules (tissue damage, scarring, inflammation)  
  (Osiecki, 2006)
Events in the Evolution of Inflammatory Acne
(Farrar, 2004, p. 382)
Acne Vulgaris

Diet & Androgens

- Androgens (endogenous or exogenous) play a large part in the pathophysiology of acne

Free androgen index is stimulated by;

- High glycaemic index (GI) diet creates hyperglycemia & reactive hyperinsulinemia.
- This in turn increases the formation of IGF-1.
- IGF-1 increases the endogenous production of free androgens.

(Tiboutot 2004)
Acne Vulgaris

Nutritional Considerations: Dairy

- Low-fat & full cream cow’s milk contains IGF-1 & IGF-2 (irrespective of pasteurisation & homogenisation).
- The equivalent level of carbohydrates in milk magnifies the insulin level by 3-6 times the amount that you would expect out of other foods.
- Whey in milk stimulates an insulin rise & casein increases the level of ILG-1. Both stimulating the production of endogenous free androgens.
- Cheese does not create this effect.
- Dairy-free ecological studies confirm this correlation.

(Danby 2010; Davidovivi 2010)
Acne Vulgaris

Treatment Aims

- Dietary assessment, modification and removal of allergens
- Hormonal balance, reduce serum androgen levels
- Assist all detoxification pathways
- Reduce inflammatory process
- Regulate blood sugar levels
- Reduce sebum production
- Maintain adequate hydration
Acne Vulgaris

Treatment Considerations
Since acne involves an inflammatory process with secondary bacterial involvement strict hygiene is beneficial in a treatment protocol:
- Washing affected areas twice a day – no scrubbing
- Complete removal of cosmetics
- Avoiding oil & wax hair products
- Avoiding picking or squeezing pimples – increases inflammation and scarring
- Moderate sunlight exposure

(Farrar, 2004),
Acne Rosacea
Acne Rosacea

- Acne Rosacea is a chronic skin disease that is characterized by erythematous, papules, papulopustules and telangiectases appearing symmetrically in the centre of the face.
- Women are more affected than men.
- Men more commonly present with rhinophyma with irreversible connective tissue and sebaceous gland hypertrophy.
- Hypochlorhydria, gastritis and ulcers have been noted.
- Several studies have suggested a potential correlation with helicobacter pylori (HP).

(Tüzün 2010)
Acne Rosacea

Second-Stage Rosacea
Rosacea begins as a redness in the face that comes and goes. If untreated, it becomes more permanent, and tiny blood vessels become visible. In addition, slight swelling, pimples and pustules develop. It can reach the point where everything that touches the face stings, burns or irritates.

(Herb-doc.com 2007)
Acne Rosacea

Ocular Rosacea
Rosacea can lead to watery, bloodshot eyes and inflammation of the eyelids. Gently scrubbing the eyelid margins with diluted baby shampoo can help relieve symptoms.

(Herb-doc.com 2007)
Acne Rosacea

Bulbous Nose Rosacea
In advanced cases of rosacea, the
nose may become bumpy, swollen and
red from excess tissue (rhinophyma).

(Herb-doc.com, 2007)
Acne Rosacea

Clinical Investigations

- CRP
- Helicobacter pylori
- Salivary Hormones
- Serum Hormones (Oestrogen, Progesterone, Testosterone)

(Kumar & Clark 2009)
Acne Rosacea

Treatment Aims

- Assess and support digestive function
- Correct hypochlorhydria
- Optimize absorption and assimilation of nutrients
- Support liver function
- Support all excretion pathways
- Reduce inflammation, support digestive mucosa
Integumentary System Nutrients & Drug Therapy
## Integumentary System

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage</th>
<th>Therapeutic Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selenium</td>
<td>200-600mcg</td>
<td>Selenium proteins (glutathione, thioredoxin reductase) are antioxidants</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>500-5,000mg</td>
<td>Increase antioxidant levels</td>
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<tr>
<td>Beta-carotene</td>
<td>15-30mg</td>
<td></td>
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<tr>
<td>Alpha-tocopherol</td>
<td>100-1000iu</td>
<td></td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>5000iu (higer psoriasis)</td>
<td>Immune regulatory and anti proliferation action</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>500-2000mcg</td>
<td>Nucleic acid synthesis, Cofactor for methionine synthetase in re-methylation of homocysteine to methionine.</td>
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(Wolters 2004; Traub 2007; Gallard 2009)
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<tr>
<td>Folate</td>
<td>1000-5000mcg</td>
<td>Cofactor for methionine synthetase in re-methylation of homocysteine to methionine. Folate is especially important for patients on methotrexate.</td>
</tr>
<tr>
<td>Essential Fatty Acids</td>
<td>1,000-6,000mg</td>
<td>Impact in kinetics of cell membranes, improve epithelial function, immune modulating through impact on eicosanoids</td>
</tr>
<tr>
<td>Chondroitin sulphate</td>
<td>1200mg</td>
<td>Support connective tissue regeneration, increases levels of anti inflammatory enzymes</td>
</tr>
<tr>
<td>Probiotics</td>
<td>10-40 Billion</td>
<td>Reduces intestinal hyper-permeability and restores gut flora. Systematic immune modulation</td>
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(Brown et al. 2004; Wolters 2004; Traub 2007; Braun & Cohen 2010; Steel 2010)
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<tr>
<td><strong>PUVA:</strong> psoralen (methoxalen) + UVA exposure</td>
<td>Oral methoxsalen is activated in UVA light to bind to DNA in the skin which suppresses skin cell division. Used in <strong>psoriasis</strong></td>
<td>Nausea &amp; itching after ingesting psoralen compound. Long term use has been associated with higher rates of skin cancer.</td>
<td>None listed</td>
</tr>
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(Bullock et al 2007)
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<tr>
<td>Topical Corticosteroid</td>
<td>Anti-inflammatory antipruritic, immuno-suppressant action.</td>
<td>Skin atrophy, striae, burning, dryness, itching, loss of pigmentation, hirsutism, folliculitis</td>
<td>Aloe vera combined with prescription creams: found to be more efficacious than just the topical cream used alone.</td>
</tr>
<tr>
<td>hydrocortisone, methyl-prednisolone, betamethasone</td>
<td>Used in psoriasis &amp; acne vulgaris to reduce topical inflammation</td>
<td>Proportion is systemically absorbed (dependent on the size of area and the frequency of application) which may result cortisol excess symptoms.</td>
<td>Green tea: concurrent consumption has presented with significant skin lesion improvements.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Zinc &amp; Biotin: co-administration of oral doses of have seen reduced requirements for topical applications of corticosteroids.</td>
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(Stargrove et al. 2008; Bryant & Knights 2011)
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<tr>
<td><strong>Oral Retinoid:</strong></td>
<td>Vitamin A derivative that inhibits sebum production &amp; is anti-inflammatory. Inhibit the growth of <em>P. acnes</em>. Used in <em>psoriasis</em> &amp; <em>acne vulgaris</em> to minimize inflammation and scarring</td>
<td>Dryness and cracking of mucosa and lips. Dry and peeling skin. Dry, itchy eyes. These side effects can be minimised by using lip balm, moisturiser, artificial tears and drinking plenty of water.</td>
<td><strong>Vitamin A:</strong> Concurrent use of Vitamin A with isotretinoin will have additive effects and increase the risk of severe adverse effects and toxicity. <strong>Grapefruit juice:</strong> drug metabolised by CYPP450 3A4, so CYP3A4 inhibitors raise plasma levels.</td>
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(Braun & Cohen 2010; Bryant & Knights 2011)
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<tr>
<td>Cytotoxic Immunosuppressant:</td>
<td>Inhibits cell replication &amp; is utilized in this instance to reduce</td>
<td>Bone marrow suppression &amp; immunosuppression</td>
<td><strong>Vitamin A &amp; E</strong>: Found to reduce drug side effects.</td>
</tr>
<tr>
<td>Methotrexate, Cyclosporine</td>
<td>immune system responsiveness.</td>
<td>Hair loss</td>
<td><strong>Methotrexate &amp; Folate</strong>: Drug action is a folate antagonist. Reduces</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GIT complaints – nausea, vomiting, ulcers, bleeding</td>
<td>drug side effects.</td>
</tr>
<tr>
<td></td>
<td>Used in <strong>psoriasis</strong> to modulate cell proliferation</td>
<td></td>
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(Bullock et al 2007; Kumar & Clark, 2009; Bryant & Knights 2010; Sarris & Wardle, 2010)
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<td>Keratolytic Topical Cream:</td>
<td>Topical agents that dissolve keratin plugs (unblock pores). May reduce the growth of <em>P. acnes.</em></td>
<td>Skin irritation: burning, stinging, pruritus.</td>
<td>None listed</td>
</tr>
<tr>
<td>salicylic acid, benzyl peroxide, azeliac acid</td>
<td>Used in acne vulgaris &amp; acne rosacea</td>
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(Bryant & Knights 2011)
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<td><strong>Topical Vitamin A Analogue:</strong> Alitretinoin</td>
<td>Topical retinoid that binds to and then stimulates intracellular retinoid receptors (anti-inflammatory &amp; immuno-modulatory). Reduces keratinocyte cytokine production &amp; leukocyte production. Regulates expression of genes that control cellular differentiation &amp; proliferation.</td>
<td>Skin irritation – burning, itching &amp; heat.</td>
<td>None listed</td>
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Used in **acne vulgaris**

(Clark 2009)
### Integumentary System

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(Bullock et al, 2007; Braun & Cohen 2010; Bryant & Knights 2011)
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Used in acne vulgaris

(Shojania 1982; Stargrove et al. 2008; Braun & Cohen 2010; Bryant & Knights 2011)
NMDC221 Session 23
Group Discussion
Case Study

45 year old female

**Presenting Symptoms**

- Presented strongly 4 weeks previously. Has had a ‘flushed face’ for years.
- Papular and pustular acne centralised on her face. ‘Butterfly rash’ across bridge of nose and onto her cheeks. This rash is made worse by the heat of a room, hot showers, hot weather and spicy foods.
- She enjoys red wine and drinks at least two glasses per night.
Case Study

Medications / Supplements

- Azeliac acid (Keratolytic Topical Cream) – applied twice daily to affected areas
- Minocycline (Tetracycline) – 250mg four times daily for 12 weeks
Case Study

Family History
- Mother: Rheumatoid arthritis, gastric ulcers
- Father: IBS, hemorrhoids.
- Sister: acne rosacea, severe PMS

Past Medical History
- Infant: long labour, forceps delivery. Bottle fed. Introduced solids at 6 months. Chronic earaches
Case Study

System Presentation

- Female Reproductive system:
  - She has a dragging sensation 2-3 days before her period. One week before she has extreme chocolate and sugar cravings, she gets angry and agitated. Her energy drops and she gets tired in the afternoon.
  - Her menstrual cycle has never been particularly regular. Day 1 of flow is heavy, presenting with dark blood, clotting and cramping. Day 3-4 the blood presents fresher, with a slightly lighter flow and no clots. Bleed lasts 6-7 day. Cycle is between 28-34 days long.
Case Study

System Presentation

- **Urinary**: urinates 6-7 x day. Begins dark and gets lighter yellow throughout the day.

- **Endocrine**: energy is 4/10. Worse part of the day – morning & in the afternoon. Best part of the day – evening when relaxing.

- **Nervous system**: easily agitated and stresses about the slightest thing. Describes herself as a ‘worrier’. When she is really stressed this affects her ability to get off to sleep (2/7 days). Generally falls asleep quickly. Dreams, snores, teeth grinds & wakes unrefreshed.
Case Study

Physical Examination Results

- **Nails**: poor capillary return, moons on thumbs and pointer fingers. Horizontal & vertical ridging. Spooning
- **Skin**: Ruddy complexion on the face, dry skin
- **Appearance**: central adiposity, slim arms & legs
- **Height**: 171cm  **Weight**: 97kg  **Waist**: Hip 0.91 (Female>0.85)  **BP**: 126/84
- **Zinc tally**: no immediate taste, tastes sour after 5-10 seconds.
## Case Study

<table>
<thead>
<tr>
<th>Time</th>
<th>Daily Dietary Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.30am</td>
<td>Bowl of Kellogg’s® Special K, milk. 1 cup of white coffee, 2 sugars</td>
</tr>
<tr>
<td>10am</td>
<td>Muesli bar – cranberry &amp; dark chocolate 1 cup of white coffee, 2 sugars</td>
</tr>
<tr>
<td>12pm</td>
<td>Chicken &amp; salad wholemeal wrap – lettuce, onion, tomato, cucumber, sprouts, butter</td>
</tr>
<tr>
<td>3pm</td>
<td>1 cup of white coffee, 2 sugars Chocolate bar</td>
</tr>
<tr>
<td>7pm</td>
<td>Grilled fish &amp; steamed vegetables (capsicum, broccoli, snow peas) on a bed of basmati rice</td>
</tr>
</tbody>
</table>

2 glasses of red wine per night  
Water: 1.5 litres  
Occasional: glass of fruit juice with breakfast (1/7 days)
Group Discussion

- Cover the development of complementary diagnosis and formulation of goals, application of goals to specific actions, identifying the nutrients related to each action, and developing a nutritional prescription.

- Consider individual nutrient dosage with clinical decisions, integrative management of each condition giving mechanisms of actions relevant for nutrient-drug interactions.

- Discuss findings in class with critical discussion
Group Discussion

- In the formulation of the goals and prescription of this case, groups are to consider the following questions:
  - What clinical investigations / tests would be relevant in the orthodox diagnosis of acne rosacea? Explain their relevance to the presentation of the symptoms.
  - What nutritional deficiencies present with this case?
  - What contra-indications present with the long-term drug use that presents with this case?
  - Have the contra-indications around these drugs been considered thoroughly in the presentation of this case?
References

References

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References

- Psoriasis, Retrieved from http://www.dermatology.co.uk/media/images/PSORIASIS_DRY_ON_ARM.jpg
- Acne vulgaris, Retrieved from http://medlib.med.utah.edu/kw/derm/mml/24820023.jpg
- Acne Vulgaris, Retrieved from http://www.caramed.de/akne/papulopu.jpg