NMDC221 Session 1: Gastrointestinal & Alimentary Disease Part I
Topic Overview

Recommended Reading
p2-16; 508-514 (prescribed text).

Gastrointestinal & Alimentary Disease Part I
- Principles and considerations in nutritional medicine management of the GIT
- Review anatomy and physiology of the GIT
- Nutritional management & consideration of drug-nutrient interactions
  - Gastro-oesophageal reflux disease (GORD)
- Class discussion of CAM
NMDC221 Introduction
Clinical decision making
Pharmacology Revision: history, pharmacology, adverse reactions, drug schedules.
Preparation for Session 3 this week.

- In Session 3 will be covering digestive disorders
- In this session you will be introduced to Outcome Measurement Tools that you will also be using in clinic.
- Please print the Gastrointestinal System Rating Scale questionnaire and bring this to class.
Gastro-Intestinal Tract
How our microbes make us who we are

- TED Talk (17.24 minutes) *How our microbes make us who we are*
- [http://www.ted.com/talks/rob_knight_how_our_microbes_make_us_who_we_are](http://www.ted.com/talks/rob_knight_how_our_microbes_make_us_who_we_are)
Gastro-Intestinal Tract

GIT Functions:

- Ingestion
- Secretion (cells within the GIT secrete up to 9L per day of various acids, buffers or enzymes into the GIT)
- Mixing and propulsion - peristalsis
- Digestion: Both mechanical and chemical
- Absorption: of macronutrients and micronutrients.
- Defecation: removal of waste
Gastro-Intestinal Tract

Features:

- Major interface between our inner and outer worlds
- Total surface area is 100 times larger than our skin
- The number of living microbes inhabiting the digestive system equals the total number of cells in our body
- The digestive system is richly supplied with nerves
- Digestive health is essential to our wellbeing
- Digestive function deteriorates with age, especially gastric acid and pancreatic output.
- GALT (gut assisted lymphoid tissue/mucosa assisted lymphoid tissue)
- Consider how you will prescribe dependent upon their digestive function – dose, form (powder, liquid, tab, cap)
Gastro-Oesophageal Reflux (GORD)
GORD

Questionnaire:-
www.aafp.org/afp/2010/0515/p1278.html

Differential Diagnosis:-
- Hiatus Hernia
- Helibacter pylori
- Peptic ulcer
- Acute and chronic gastritis
- Oesophageal cancer
- Gallstones
Gastro-Oesophageal Reflux

• The primary protective factor from GORD is the LES (Richter J 2007)
  o Oesophageal mucosa is exposed to gastric contents for prolonged periods of time.
  o Symptoms include heartburn, regurgitation (worse for bending, straining or lying down) and ‘water brash’.
    (Kumar & Clark, 2005, pp. 275-276)

(Tortora & Grabowski, 2003, p.861)
GORD - Signs and Symptoms:-

- ‘GORD = ‘a condition that develops when the reflux of stomach contents causes troublesome symptoms or complications.’

- There is no gold standard test for GORD. Based on symptoms experienced and/or results of tests performed.

- Patients may be diagnosed on symptoms alone or with tests demonstrating reflux of contents (e.g. testing) or by the injurious effects of the reflux (e.g. via endoscopy).

(Richter, 2007)
GORD – Signs and symptoms adults:

- May be worse at night (undigested food from late/large meals and delayed gastric emptying causes increased intra-abdominal pressure and distension of the stomach)
- Atypical chest pain can mimic angina and is probably due to reflux induced oesophageal spasm.
- May develop oesophagitis, odynophagia & / or dysphagia (Kumar & Clark, 2005, pp. 275-276)

- 20-40% adults present with GORD at least 1x week (Mahan & Escott-Stump, 2009, p.656).
- The condition is a relapsing and remitting disorder
Signs and symptoms infants -

• Excessive crying is the most prevalent reason for an infant visiting the doctor in the early stages of life affecting approx. 30% babies (Douglas, 2005).

• And approx. 50% of infants in the first years of life present with GORD, most resolving in the first year of life (Mahan & Escott-Stump, 2008, p.656).

• Excessive crying can predispose infant to GORD after approx. 3-4 months of age (Douglas, 2005). Therefore look at feeding practices (overfeeding, possible cows milk allergy, referral to lactation consultant); sensory nourishment (baby wearing); parental responsiveness (reading baby cues); sleep management (co-sleeping, adequate rest) all important considerations.
Gastro-Oesophageal Reflux - Infants Cont.

Excessive crying and GOR in infants.

(Douglas P 2005)

INFOGRAPHIC:

**FEEDING MANAGEMENT**
- Consider:
  - frequent feeds

**PARENTAL RESPONSIVENESS**
- Consider:
  - prompt parental response to cues
  - maintaining exchange of sensory data: infant in same room as caregiver

**SENSORY NOURISHMENT**
- Consider:
  - sling/backpack
  - outdoor walks
  - increased social contact
  - massage
  - comfort eg tight nappy? irritating garment? overdressing?

**SLEEP MANAGEMENT**
- Consider:
  - nocturnal co-sleeping
  - sensory nourishment instead of daytime sleep struggle

**TRIAL PROTON PUMP INHIBITOR**
- in addition to consideration of feeding management, parental responsiveness, sensory nourishment and sleep management

- If > 3-4 months and persistently vomiting

- If breast fed and symptoms continue
  - Consider:
    - weight gain
    - relative proportion of fore and hind milk
    - attachment and positioning
    - abandon burping rituals

- Prompt referral to Lactation Consultant
  - Trial elimination of dairy products from maternal diet

- If symptoms of cow’s milk allergy
  - Referral to paediatrician
    - (hydrolysed protein or amino acid formula)
  - ?Referral to Lactation Consultant (relactation)

- If crying continues
  - Referral to paediatric gastroenterologist
    - (endoscopy)
Prevalence of GORD:-

- In the western world, prevalence generally ranges between 10% and 20%.
- In Asia, the prevalence is reported to be less than 5%.
- There is a trend for the prevalence to be higher in North America than in Europe (Richter, 2007)
Risk Factors

- Weight (BMI >25) was associated with a 2.5-3 fold increase in symptoms (Corley & Kubo, 2006); erosive esophagitis and oesophageal adenocarcinoma, gastric cardia adenocarcinoma (Nilsson et al. 2003; Hampel et al. 2005); risk of these disorders increased with increasing weight.

- Helibacter pylori. There’s a negative association between h. pylori and GORD as seen in Asian countries which have a lower incidence of GORD and western countries, a higher incidence (Richter, 2007).

- Transient lower oesophageal sphincter (LES) relaxation and spatial separation of the LES diaphragm (hiatus hernia) (Richter, 2007).

- Smoking – reduction of LES pressure (Mahon, Escotee-Stump & Raymond, 2012);

- Genetics

- Drugs - HRT exacerbated symptoms of GORD (Nilsson et al. 2003; Hampel et al. 2005)
Gastro-Oesophageal Reflux

Therapeutic Actions Adults:-

- Minimise or manage foods / agents that reduce sphincter tone. These include –
  - Chocolate, fatty meals, carminatives (spearmint, peppermint), smoking, alcohol.
  - Drugs (calcium channel blockers, diazepam, theophylline)
  - Hormones (oestrogen, progesterone)
  - Physiologic factors (e.g. prostaglandin, glucagon, vasoactive intestinal peptide) (Mahan & Escott-Stump, 2008, p. 657)

- Include - antioxidant rich foods, legumes and whole grains, chamomile, cinnamon, ginger. These aid in regulating GIT motility, act as anti-inflammatory and anti-microbial agents and may reduce nausea and excessive salivation. Cabbage and cabbage juice aid the healing of irritated tissue from acid regurgitation (Sarris & Wardle, 2010, pp. 78-79).
Gastro-Oesophageal Reflux

Therapeutic Actions

- Manage issues with reduced swallowing capacity:
  - Neurological disorders (e.g. stroke)
  - Decreased saliva production (e.g. elderly, anticholinergics)
- Manage any issues with delayed gastric emptying:
  - Fatty meals
  - Lying down within 45 minutes of eating
  - Diabetes

(Mahan & Escott-Stump, 2008, p. 657)
Gastro-Oesophageal Reflux

Therapeutic Actions

- Minimize agents that increase acid production:
  - Smoking – prolongs acid clearance. Higher rate of GERD in smokers versus nonsmokers.
    (Watanabe et al. 2003)
  - Drugs (e.g. NSAIDs, aspirin)
  - Foods and beverages e.g. coffee, tea, carbonated drinks, chocolate, citrus, spicy foods

- Minimize irritant effects on the oesophagus:
  - Drugs (e.g. tetracycline's, iron salts, aspirin, NSAIDs)
  - Foods (e.g. citrus foods, tomatoes, coffee)
    (Mahan & Escott-Stump, 2008, p. 657)
Gastro-Oesophageal Reflux

Therapeutic Actions – infants

- Consider feeding practices; check sleep quality and quantity; baby cues; mothers diet in b’fed infant (high in dairy or chocolate); feeding position


- Maternal or infant dairy-free diet may be beneficial. Supplement with soy, goat milk alternatives or extensively hydrolysed whey formula

- Carob bean gum (0.33mg/100ml formula) powder has been found to decrease the severity and frequency of GORD. Contains galactomannans which protect from acid (Georgieva et al 2016).

(Sarris & Wardle, 2010, p 78-9)
Key nutrients to consider

- Slippery Elm
- Glutamine
- Betaine hydrochloride
- Aloe Vera (inner leaf juice)
- Vitamin C
- Probiotics (*L. rhamnosus*; *B. infantis*)
- Cabbage juice
### Slippery Elm in Gastro-Oesophageal Reflux

<table>
<thead>
<tr>
<th>Mechanism of action</th>
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| • Contains high amounts of mucilage → traps water to form a gel-like substance.  
• Gel-like substance adheres to the mucous membranes and forms a barrier against stomach acid → preventing pain, ulceration and cellular changes (Braun, 2006). |

<table>
<thead>
<tr>
<th>Evidence of clinical application</th>
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| • First used by Native Americans as a healing salve for wounds, ulcers and inflammation (UMMC, 2014)  
• There have been no scientific studies done on the use of Slippery elm bark and GORD, however there is a significant amount of traditional and empirical evidence supporting its use. |

<table>
<thead>
<tr>
<th>Dosage</th>
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| **Acute:** 1500 - 2000mg per day, for 4 – 8 weeks. An additional 400 – 500mg can be taken if acute pain is being experienced. (UMMC, 2014)  
**Chronic/Maintenance:** 800 – 1500mg per day. |

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<tr>
<th>Other considerations</th>
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| • Contraindicated in pregnancy.  
• Can be made as a tea or taken as a powder. Also prescribed in capsules.  
• There is a theoretical concern that because it lines the digestive tract, it might affect the absorption of drugs. Separate the dosage by 2 hours. (Braun, 2006) |
# Glutamine in Gastro-Oesophageal Reflux

| Mechanism of action | • A key nutrient for rapidly proliferating cells  
|                     | • Reduces oxidative damage  
|                     | • The preferred respiratory fuel for enterocytes – vital in maintaining a healthy intestinal lining  
|                     | • Maintain secretory IgA production → Antimicrobial (especially if GORD is being driven by *H. pylori* overgrowth) (Braun & Cohen, 2010) |
| Evidence of clinical application | • Although commonly prescribed for GORD, there are no large scale or specific studies on glutamine supplementation and GORD. Much of the clinical application has come from extrapolating data and actions identified in studies done on other gastrointestinal conditions.  
|                     | • Despite this, glutamine has been shown to be effective in a clinical setting and based on the mechanism of action, is often prescribed by naturopaths and holistic nutritionists. |
| Dosage | Best taken as a powder formulation. 4 – 6 grams per day, in divided doses. (i.e. 2 – 3g, twice a day) (Braun & Cohen, 2010) |
| Other considerations | None |
### Betaine Hydrochloride in Gastro-Oesophageal Reflux

| Mechanism of action | • “Betaine hydrochloride supports the pH decline in the stomach thereby, potentially improving nutrient digestibility”
|                     | Betaine has shown an anti-apoptotic effects and promotes cell proliferation.
|                     | - Betaine accumulates in cell organelles and replaces inorganic ions, allowing protective enzymes and the cell membranes to remain viable.
|                     | - The chloride component is directly used to increase stomach acid production. (Eklund et al. 2005) |
| Evidence of clinical application | • “If low stomach acid is the cause of reflux symptoms, betaine hydrochloride may be useful.” (Hechtman, 2012)
|                     | - There are no studies on betaine hydrochloride supplementation and the effects on Gastro-oesophageal reflux. Clinical application has developed from assessing the underlying drives of GORD and the biochemical pathways of betaine hydrochloride. |
| Dosage | • There is no typical dosage for betaine hydrochloride. Practitioners should follow manufacturers guidelines. |
| Other considerations | • “Betaine hydrochloride should only be taken with protein containing meals and the dose should be built up slowly”. (Hechtman, 2012)
|                     | • Patients may feel a warming sensation in their abdomen. This should be relieved by food. |
**Aloe Vera in Gastro-Oesophageal Reflux**

| Mechanism of action | Contains a glycoprotein fraction that increases the expression of receptors and cell proliferation to enhance wound healing (*in vivo*).  
|                     | “Aloe contains 2 dihydroisocoumarins that demonstrate free radical scavenging properties. This is also supported through the inclusion of flavonoids and polysaccharides which supports healing and antioxidant activity” (Braun & Cohen, 2010) |

| Evidence of clinical application | “The gel reduces oxidation of arachidonic acid and as such, prostaglandin formation → anti-inflammatory.”  
|                                | “A study in rats found that aloe gel reduced vascularity and swelling by 50% in inflamed synovial pouches”. (Braun & Cohen, 2010) |

| Dosage | Best administered as a liquid gel.  
|        | Start with 25 – 50mls, twice per day to test for tolerance. Can go up to 100mls, twice per day in more severe cases (Langmead et al. 2004) |

| Other considerations | Generally well tolerated, although some preparations contain the latex, which has a laxative effect. |
### Vitamin C in Gastro-Oesophageal Reflux

#### Mechanism of action
- Vitamin C is an electron donor, accounting for most of its biological functions → anti-oxidant.
- Adequate vitamin C status prevents degranulation of tissue and allows for adequate wound healing.
- Assists with the proper formation of collagen, elastin and fibronectin, thereby helping to improve sphincter tone. (Braun & Cohen, 2010)

#### Evidence of clinical application
- There is evidence to suggest that a vitamin C deficiency exists in gastric diseases. Further to this, the overgrowth of *H. pylori* has been shown to contribute to creating this deficiency (Aditi & Graham, 2012).
- Very limited studies of vitamin C administration for GORD are available.

#### Dosage
- 500mg twice per day (Hechtman, 2012)

#### Other considerations
*The degree of the absorption depends on the dose ingested and decreases as the dose increases. At a low concentration most vitamin C is absorbed by the sodium vitamin C co-transporter 1 in the small intestine and reabsorbed in the renal tubule. At high concentrations, these transporters become saturated, limiting the amount that can be absorbed.* (Braun & Cohen, 2010)
## Other nutrient considerations:

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage</th>
<th>Therapeutic Actions</th>
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<tbody>
<tr>
<td>Digestive enzymes</td>
<td>Enzymes with food (dose varies on product)</td>
<td>Improves food breakdown, increases nutrient absorption</td>
</tr>
<tr>
<td>Selenium</td>
<td>25-250mcg</td>
<td>Deficiency has been linked to the progression of Barrett’s oesophagus</td>
</tr>
<tr>
<td>Zinc</td>
<td>10-100mg/day</td>
<td>Deficiency is linked to Barrett’s oesophagus and the risk of oesophageal adenocarcinoma. Increase would healing</td>
</tr>
<tr>
<td>Omega 3 Fish Oil</td>
<td>1-6gm /day</td>
<td>Anti-inflammatory</td>
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(Mahan & Escott-Stump, 2008, p. 658; Sarris & Wardle, 2010, p. 77)
## Gastro-Oesophageal Reflux

<table>
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<th>Drug</th>
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<th>Side Effects</th>
<th>Interaction</th>
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<tbody>
<tr>
<td>OTC Antacids</td>
<td>Neutralizes acid by increasing bicarbonate and mucous. Inactivates pepsin. Binds bile salts</td>
<td>Diarrhoea (Mg), constipation (Al), hypophosphataemia (with low phosphate intake), hypercalcaemia</td>
<td><strong>Vitamin C</strong>: increases aluminium absorption. Separate doses by 2 hrs. <strong>Folate &amp; Iron</strong>: reduces absorption of both. Separate doses by 2 hours</td>
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(Braun & Cohen, 2010, p1096; Bryant & Knights, 2011, p. 538)
# Gastro-Oesophageal Reflux

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<td><strong>‘Raft’ Antacids:</strong></td>
<td>Mixes with stomach acid forms a slimy jelly ‘raft’ reducing acid, pepsin &amp; bile acids on mucosa</td>
<td>Low incidence of side effects (less than 5%). Constipation</td>
<td>Vitamin E &amp; Calcium: reduces absorption of both</td>
</tr>
<tr>
<td><strong>Alginic Acid</strong></td>
<td></td>
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<tr>
<td><strong>Sucralfate</strong></td>
<td>Increases bicarbonate and mucus production, localized PG release = repair of gastric mucosa</td>
<td>Sucralfate: nausea, headache, rash, dizziness &amp; indigestion.</td>
<td>Vitamin E &amp; Calcium: reduces absorption of both</td>
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(Braun & Cohen, 2010, p1096; Bryant & Knights, 2011, p. 538)
# Gastro-Oesophageal Reflux

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<tr>
<td><strong>H2-Antagonist</strong></td>
<td>Blocks H2 receptors on parietal cells. Reduce amount, and dissolution of gastric acid raises pH and reduces the activity of pepsin</td>
<td>Diarrhoea, nausea, constipation, headache, dizziness, skin rash</td>
<td><strong>Folate, B12 &amp; Iron</strong> : reduces absorption of both. Separate doses by 2 hrs.</td>
</tr>
<tr>
<td><strong>Proton Pump Inhibitors</strong></td>
<td>Reduces gastric output via non-competitive &amp; irreversible bonds with H+/K+ ATPase on parietal cells. Action lasts for days after stopping the drug.</td>
<td>Diarrhoea, nausea, abdominal pain, headache. Sustained reduction of HCl causes increase in gastrin.</td>
<td><strong>Folate B12 &amp; Iron</strong> : reduces absorption of both. Separate doses by 2 hrs.</td>
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(Braun & Cohn, 2010, p. 1097; Bryant & Knights, 2011, pp. 541- 543)
# Gastro-Oesophageal Reflux

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<th>Action</th>
<th>Side Effects</th>
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<tr>
<td><strong>Dopamine 2 Antagonists:</strong></td>
<td>Inhibition effect on dopamine = reduced gut motility. Increases gastric emptying. Increases lower oesophageal sphincter tone</td>
<td><strong>Metaclopramide:</strong> drowsiness, fatigue, nervousness, anxiety, diarrhoea, insomnia.</td>
<td>None found</td>
</tr>
<tr>
<td>Metaclopramide</td>
<td></td>
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<tr>
<td>Domperidone</td>
<td>As above</td>
<td><strong>Domperidone:</strong> less side effects (minimal BBB crossover)</td>
<td>None found</td>
</tr>
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(Bryant & Knights, 2011, p. 541)
Clinical Decision Making
Clinical Decision Making

A decision-making framework aids in generating a step-by-step case management system.

A decision making checklist for a case would include:
- Highlight important case points
- Create answerable clinical questions
- Construct a research strategy
- Formulate treatment protocol
- Self-evaluate

(Leach, 2010, p. 7)
Clinical Decision Making

- The number of visits to Complementary and Alternative Medicine (CAM) practitioners by adult Australians in a year (69.2 million) was almost identical to the estimated number of visits to medical practitioners (69.3 million).

- Less than half of these adult Australians informed their medical practitioners that they used CAM (Xue, Zhang, Lin, Da Costa & Story, 2007, p. 650).
Clinical Decision Making

Discussion

Based on the previous points raised by the study conducted by Xue et al. (2007):


What are the ramifications if less than half of our clients are willing to discuss with their GP that they are taking supplementation that may interact with their prescription medication?
Clinical Decision Making

Outcomes associated with use of dietary modification and nutraceuticals with prescription drugs:

• Reduced drug effect
• Added drug effect
  • Increased or decreased incidence of adverse effects
• Synergistic effect that is beneficial or negative
• Improvement in overall treatment of disease process
  • Restore tissues that may be adversely affected by drug
  • Reduced side effects associated with drug
  • Arrest nutrient deficiencies associated with drug
  • Reduce drug dose overtime

(Braun & Cohen, 2010, p. 94)
Clinical Decision Making

Integrated Treatment Approach
Combined use of drug, herb &/or nutrient safety depends on:

- Predicted potential for an interaction
- Appropriate use of each intervention (dose, indication, route of administration, timing of administration etc…)

(Braun & Cohen, 2010, p. 104)
Clinical Decision Making

Integrated Treatment Approach

Risk Rating - drugs most likely to have interactions are:
  o Drugs with a narrow therapeutic window
  o Drugs that are anti-coagulants, anti-hypertensives, anti-diabetic, anti-psychotic and anti-epileptic drugs

Patients at most risk of interactions are:
  o Elderly
  o Children
  o Patients with impaired renal or liver function

(Braun & Cohen, 2010, p. 105-106)
Clinical Decision Making

Integrated Treatment Approach

When taking a client's case (initial and repeat) review the following points:

- Ask about the use of all CAM, over-the-counter (OTC) and prescription medications: including practitioner prescribed and self-medicated
- Consider the age, sex and genetic predispositions of your patient.
- Concurrent disease states may have an effect on absorption, distribution, metabolism and excretion

(Braun & Cohen, 2010, p. 123)
Clinical Decision Making

Integrated Treatment Approach
- Refer to drug information centres, peer-reviewed literature, reputable sources for information
- Document relevant information and recommendations on case notes
- Suspend the use of nutrients or herbs 5-7 days before surgery or childbirth, where appropriate
  (Braun & Cohen, 2010, p. 123)
Pharmacology: Revision
Phases Affecting Drug Activity

Administration of Drug

PHARMACEUTICAL PHASE
Drug is dissolved

Available portion of the drug is absorbed

PHARMACOKINETIC PHASE
Drug moves into the bloodstream

Drug is available for distribution

Drug distributed to organs & tissues

PHARMACODYNAMIC PHASE
Drug-molecular target interaction

Drug Effect

Drug metabolized & / or excreted

Elimination

(Bryant, Knight & Salerno, 2007, p 112)
Pharmacology

Pharmacokinetics: What the body does to the drug.

- **Absorption**: when the drug presents in the bloodstream.
- **Distribution**: once the drug is in the bloodstream (absorbed) it is then distributed to high blood flow areas (heart, kidneys, liver). Partial barriers include the Blood Brain Barrier (BBB) & placenta.
- **Metabolism**: modification of a drug (usually by enzymes) into less active products.
- **Excretion**: metabolized drug leaves the body

(Bryant & Knights, 2011, p. 2)
Pharmacology

Pharmacodynamics: How & what the drug does to the body

- The biochemical & physiological effects, mechanism of action and adverse effects of the drug
- Potency, selectivity & specificity of the drug needs to be considered when exploring the magnitude of effect and adverse effects.
- Drug receptor responses include agonists, partial agonists, antagonists, negative antagonists, competitive antagonists or irreversible antagonists

(Bryant & Knights, 2011, p. 2)
Integrative Interactions
Pharmacology

Pharmacokinetic Interactions

- Occur when the combination of drug-drug, drug-herb or drug-nutrient results in any alteration in absorption, distribution, metabolism or excretion.

- Can be positive or negative and relate to the duration or magnitude of drug effect, rather than the type of effect.

  (Braun & Cohen, 2010, p. 95)
Pharmacology

Pharmacokinetic Interactions: Absorption
Orally administered drugs can be affected by the rate or extent of drug absorption.
This includes;
- Alteration to gut motility
- Physical barriers – mucilage
- Gastric acid alteration
- Cell membrane responses – P-glycoprotein

(Braun & Cohen, 2010, p. 95)
Pharmacology

Pharmacokinetic Interactions: Absorption via P-gp

- **P-glycoprotein** transports drugs out of cells.

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<tr>
<th>Inhibition of P-gp</th>
<th>Induction of P-gp:</th>
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<tbody>
<tr>
<td><strong>Reduced</strong> cell excretion of the drug = increased absorption, distribution &amp; bioavailability</td>
<td><strong>Increased</strong> cell excretion of the drug = reduced absorption, distribution &amp; bioavailability.</td>
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</table>

**Agents:**
- Grapefruit, orange, apple juice
- Rosemary extract
- Genistein & diadezein
- Resveratrol, quercetin, green tea polyphenols
- Piperine (black pepper)

**Agents**
- St John’s wort
- Genistein & diadezein (soy isoflavones)

(Braun & Cohen 2010, p. 96; Rakel 2007)
Pharmacology

Pharmacokinetic Interactions: Metabolism

Alteration to liver metabolism will affect how much drug reaches systemic circulation.

- Enzymes CYP1A2, CYP2D6, CYP3A4 metabolize over 50% of most drugs in the liver

<table>
<thead>
<tr>
<th>Inhibition of CYP enzyme</th>
<th>Induction of CYP enzyme</th>
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<tr>
<td><strong>Reduced</strong> metabolism = increased drug concentration in the blood</td>
<td><strong>Increased</strong> metabolism = reduced drug concentration in the blood</td>
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Agents:
- Grapefruit juice, garlic oil
- Cruciferous vegetables, char-grilled meat, high-protein diets, alcohol, St John’s wort

(Braun & Cohen, 2010, p. 98)
Pharmacology

Pharmacokinetic Interactions: Metabolism

Phase I Metabolism
- Cytochrome P450 enzymes require adequate levels of copper, magnesium, zinc and vitamin C
- Glutathione is the most important endogenous antioxidant neutralising free radical toxic metabolites

Phase II Metabolism
- A wide range of nutrients are required to support efficient Phase II detoxification including an adequate level of essential and non-essential amino acids

(Braun & Cohen, 2010, p. 100)
Pharmacology

Pharmacokinetic Interactions: Excretion
Kidneys are the major organ of excretion. Factors that alter renal excretion include;
- Altered tubular reabsorption or glomerular filtration rate
- Changes to renal tubule mucous
- Competition for absorption via membrane transporter proteins
- Altered urine pH will
- Acidify: high doses of Vitamin C
- Alkalize: low-protein diets, ingestion of potassium citrate

(Braun & Cohen 2010, p. 101)
Pharmacology

Pharmacodynamic Interactions
Interaction between agents by altering the sensitivity or response of target tissue.
Pharmacodynamic Responses can be;
- Additive: magnify the response
- Synergistic: combined increase a positive outcome
- Antagonistic: reduces the effectiveness of one agent
- Note: Need to consider dosages, patient idiosyncrasies and the timeframe of usage

(Braun & Cohen, 2010, p. 101)
Physiochemical Interactions

- Interaction between two or more agents before absorption. E.g. Vitamin C & non-haem iron, mucilage (slippery elm, psyllium), similar mineral ions compete for absorption, tannins binding to proteins, nitrogenous bases, polysaccharides & metal ions

Chelation Interactions

- Interaction between a metal ion and another substance leading to reduced activity or inactivation of the mineral and/or drug. E.g.. Oxalates and phytates

(Braun & Cohen, 2010, p. 102)
Pharmacology

Disease Interactions
- When a substance alters a disease state
- Positive effects. E.g. Glucosamine and osteoarthritis
- Negative effects. E.g. pregnancy and various substances (Braun & Cohen, 2010, p. 90)

Iatrogenic Interactions
- Is the presentation of cumulative symptoms when a drug is given to counter the adverse effects of another drug. E.g. Codeine → constipation → use of laxatives)
Pharmacology

Integrative and Adverse Reactions Review

- There is little information on the potential interactions between drugs, nutritional or food therapies

- Currently, these interactions are poorly documented and reported by both medical and natural health practitioners

- Not all interactions are clinically significant. Many drug-herb and drug-nutrient interactions are currently theoretical, with no definitive evidence available.

(Braun & Cohen, 2010, p. 106)
Pharmacology

Integrative and Adverse Reactions Review

- Much of the current data on drug-herb-nutrient interactions is based on *in vitro* studies. More evidence will emerge over time.

- Potentially serious or harmful reactions are often limited to small patient numbers. However, serious interactions can occur and may lead to hospitalization.

  (Braun & Cohen, 2010, p. 106)
Integrative and Adverse Reactions Review

- When interpreting reports of interactions or adverse reactions between a drug and herbal/nutritional therapy, consider the following;
  - Possibility of extrinsic factors (e.g. interaction is due to contaminants not natural therapy)
  - The degree of certainty that this is valid interaction
  - Clinical relevance

(Braun & Cohen, 2010, p. 106)
Pharmacology

Integrative and Adverse Reactions Review

We can reduce the risk of negative interactions by:

- Taking a thorough patient medication history
- Researching all drugs and potential interactions before prescribing herbs and nutrients
- Becoming familiar with the most likely and potentially serious interactions
- Using reliable references for information on both drug therapy and drug-herb/nutrient interactions
- Consult other healthcare professionals where needed

(Braun & Cohen, 2010, p. 92)
## Drug & Poison Schedule

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Pharmacy medicine: requiring professional advice for sale</td>
</tr>
<tr>
<td>3</td>
<td>Pharmacist only: requires professional advice from a pharmacist</td>
</tr>
<tr>
<td>4</td>
<td>Prescription only: requires a prescription for dispensing by a Pharmacist</td>
</tr>
<tr>
<td>5</td>
<td>Caution: drug has potential to cause harm so relevant warnings and directions are required</td>
</tr>
<tr>
<td>6</td>
<td>Poison: drug has a moderate potential to cause harm. Requires schedule specific packaging with strong warnings and safety directions.</td>
</tr>
<tr>
<td>7</td>
<td>Dangerous Poison: drug has significant potential for causing harm with minimal exposure. Requires specific precautions in manufacturing, handling &amp; use. Restricted / authorized users, availability, possession, storage requirements &amp; use apply.</td>
</tr>
<tr>
<td>8</td>
<td>Controlled drug: drug of potential misuse, abuse &amp; dependence. Restriction of manufacture, supply, distribution &amp; possession.</td>
</tr>
<tr>
<td>9</td>
<td>Prohibited substance: manufacture, possession, sale or use is prohibited by law unless required for medical/scientific purposes.</td>
</tr>
</tbody>
</table>

(Bryant & Knights, 2011, p. 1025)
## Drug-in-Pregnancy Risk Category

<table>
<thead>
<tr>
<th>Cat.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Taken by high # of women (pregnant/fertile age) with no proven harmful effects on fetus</td>
</tr>
<tr>
<td>B</td>
<td>Taken by a limited # of women (pregnant / fertile age) with no proven harmful effects on fetus</td>
</tr>
<tr>
<td>B1</td>
<td>Taken by a limited # of pregnant /childbearing age women with no harmful effects on fetus. Animal trials show no evidence.</td>
</tr>
<tr>
<td>B2</td>
<td>Taken by a limited # of pregnant /childbearing age women with no proven harmful effects on the fetus. Animal studies lacking but limited # shows no evidence of increased fetal damage</td>
</tr>
<tr>
<td>B3</td>
<td>Taken by a limited # of pregnant /childbearing age women with no proven harmful effects on fetus. Animal studies have shown evidence of fetal damage but with no correlation to human fetus identified.</td>
</tr>
<tr>
<td>C</td>
<td>Caused / theoretically could cause fetal harm without malformation. Reversible results.</td>
</tr>
<tr>
<td>D</td>
<td>Caused / theoretically could cause a high occurrence of fetal malformation or irreversible damage.</td>
</tr>
<tr>
<td>X</td>
<td>High risk of causing irreversible damage. Don’t use in pregnancy or possibility of pregnancy</td>
</tr>
</tbody>
</table>

(Braun & Cohen, 2010, p. 164)
Group Discussion

- How many people do you know that take some form of supplements?
- How many people do you know take prescription medication?
- What is the relevance of integrating pharmacology with nutritional understanding?
References


References


References


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