NMDC221 Session 5: Hepatic Disease
Topic Summary

Liver Detoxification Pathways

- Nutritional management of liver detoxification pathways, alcoholic liver disease, steatosis (fatty liver), hepatitis A,B,C.
- Nutritional support and modulation of hepatological disorders
- Therapeutic diet: reduced-fat diet
- Relevant nutrient-drug interactions
Recommended Reading
Pg. 360-1; 560-84(prescribed text).
Liver Detoxification Pathways

Liver Filtering and Functions

- Filters and detoxifies the blood (1.5 L/minute) from the GIT (portal vein) for hepatic first pass clearance.

- **Phase I:** Lipid soluble toxins & chemicals convert to intermediate metabolites via cytochrome P450 enzymes. Metabolites are then excreted or proceed to phase II liver clearance.

- **Phase II:** addition of amino acids to phase I metabolites makes the molecules more water soluble and easier to eliminate (bile in stool, urine, sweat, exhaled)

(Baker et.al. 2006; Katzung, 2007; Mahan & Escott-Stump, 2008, p.708; Sarris & Wardle, 2010)
FIG 1. Liver Detoxification Pathways and Supportive Nutrients

Toxins → Step 1 → Step 2 → Waste Products
(fat soluble) (water soluble)

Phase I Required Nutrients
- Folic Acid
- Vitamin B3
- Vitamin B6
- Vitamin B12
- Vitamin A
- Vitamin C
- Calcium
- Vitamin D3
- Vitamin E
- Milk Thistle
- N-acetyl Cysteine
- Citrus Bioflavonoids
- Quercetin

Phase II Required Nutrients
- Calcium D-glucarate
- Amino Acids:
  - L-glutamine
  - L-lysine HCL
  - Glycine
  - L-carnitine
  - Taurine

Cruciferous vegetables
(Sulfur metabolites)
- MSM
- N-acetyl Cysteine

Eliminated from the body via:
- Gallbladder
- Bile
- Bowel actions
- Kidneys
- Urine

Toxin List
- Metabolic end products, micro-organisms,
- contaminants / pollutants, insecticides,
- pesticides, food additives, drugs, alcohol
Liver Detoxification Pathways

Phase I Detoxification

- Alters functional groups on lipid soluble molecule inactivating or, in pro-drug cases, activating them.
- All chemicals within the body pass through this reaction.
- CYP 450 is a generic name for a family of enzymes:
  - Family number – CYP1, CYP2 & CYP3
  - Sub-family letter – A, B, C, D
  - Followed by another number based on the gene that it presents on

(Braun & Cohen, 2010)
# Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>CYP</th>
<th>Metabolized Substrate Examples</th>
<th>Inducers</th>
<th>Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A2</td>
<td>Caffeine, Clozapine, Melatonin, Naproxen, Paracetamol, Theophylline, R-warfarin</td>
<td>Smoking, charcoal-broiled foods, cruciferous vegetables.</td>
<td>Genistein and daidzein in vitro</td>
</tr>
<tr>
<td>2B6</td>
<td>Amitriptyline, Diazepam, Methadone, Tamoxifen, Temazepam, Testosterone</td>
<td></td>
<td>Grapefruit juice</td>
</tr>
<tr>
<td>2C19</td>
<td>Diazepam, Omeprazole, Sertraline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D6</td>
<td>Beta-blockers, Codeine, Fluoxetine, Haloperidol, Nicotine, Metoprolol, Tamoxifen, Tramadol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2E1</td>
<td>Alcohol</td>
<td>Ethanol</td>
<td>Garlic</td>
</tr>
<tr>
<td>3A4</td>
<td>Caffeine, Calcium channel blockers, Codeine, Cyclosporin, Erythromycin, Oestradiol, Progesterone, Tamoxifen, Testosterone</td>
<td></td>
<td>Peppermint (in vitro) Grapefruit, oranges, star fruit, pomegranate</td>
</tr>
</tbody>
</table>

(Katzung, 2007; Nekvindová & Anzenbacher, 2007; Braun & Cohen, 2010)
Liver Detoxification Pathways

Phase I: CYP Enzymes

The enzymes **CYP1A2, CYP2D6, CYP3A4** are responsible for the **metabolism of over 50% of most medicines**

**Interactions:**

- Drugs with a narrow therapeutic index are most affected by changes to CYP enzyme activity as there is a greater risk of toxicity or sub-therapeutic dosing
- **Inducers** will accelerate drug metabolism and reduce blood levels
- **Inhibitors** will slow down drug metabolism and increase blood levels

(Braun & Cohen, 2010)
# Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Phase I Requirement</th>
<th>Nutrient</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP are heme containing compounds</td>
<td>Iron</td>
</tr>
<tr>
<td>Required for phase one detoxification</td>
<td>Copper, Magnesium, Zinc, Vitamin C, Vitamin B1, Vitamin B3 (NADH)</td>
</tr>
</tbody>
</table>

- **Liver Antioxidant**
  - A component of glutathione
  - Co-factor for glutathione peroxidase
  - Glutathione
  - Cysteine, Glutamic Acid, Glycine
  - Selenium

*Osiecki, 2006; Stargrove, Treasure & McKee, 2008*

Glutathione substrates are important for Phase I and Phase II detoxification.
Liver Detoxification Pathways

Nutritional Considerations

Phase I

- The 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
- Thus optimising nutrient intake, whether through dietary sources or nutritional supplements will enhance the liver’s ability to metabolise drugs efficiently
- Additionally, polypharmacy depletes glutathione

( Osiecki, 2006)
Liver Detoxification Pathways

Nutritional Considerations

Phase II Detoxification

○ Phase I can create free radicals as part of the detoxification process

○ Phase II detoxification is required to occur at an adequate level to maintain detoxification of these phase I “...intermediate metabolites, endogenous carcinogenic intermediates and reactive oxygen intermediates...”

○ Phase II enzymatic pathways require appropriate nutritional, rate limiting co-factors

(Osiecki, 2006, p.117; Sarris & Wardle, 2010)
Liver Detoxification Pathways

Nutritional Considerations
Phase II detoxification: six pathways
- Glutathione Conjugation
- Methylation
- Sulphation
- Acetylation
- Glucuronidation
- Amino acid conjugation

(Baker et.al. 2006)
# Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Glutathione</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug metabolized eg.</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen, Paracetamol</td>
<td>Penicillin, Tetracycline</td>
</tr>
<tr>
<td>Xenobiotics</td>
<td></td>
</tr>
<tr>
<td>Toxic Metals</td>
<td>Aromatic hydrocarbons: ie. napthalene, anthracene</td>
</tr>
<tr>
<td>Petroleum Distillates</td>
<td></td>
</tr>
<tr>
<td>Dietary/ Endogenous</td>
<td></td>
</tr>
<tr>
<td>Bacterial Toxins, Aflatoxin</td>
<td>Quercetin, N-AC</td>
</tr>
<tr>
<td>Lipid Peroxides</td>
<td>PG’s &amp; LT’s</td>
</tr>
<tr>
<td>Ethyl Alcohol</td>
<td>Bilirubin</td>
</tr>
<tr>
<td>Nutrients required</td>
<td></td>
</tr>
<tr>
<td>Glutathione (100-500mg)</td>
<td>Vitamin B2 (10-40mg)</td>
</tr>
<tr>
<td>Cysteine (200-500mg)</td>
<td>Vitamin B6 (10-150mg)</td>
</tr>
<tr>
<td>Glutamine (0.5-3gm)</td>
<td>Vitamin C (250-1000mg)</td>
</tr>
<tr>
<td>Glycine (200mg/kg)</td>
<td>Selenium (100-200mcg)</td>
</tr>
<tr>
<td>Methionine (adult 13mg/kg)</td>
<td>Zinc (10-100mg)</td>
</tr>
</tbody>
</table>

(Osiecki, 2006; Bryant & Knights, 2007; Sarris & Wardle, 2010)
# Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Methylation</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug metabolized e.g.</td>
<td>Thiouracil</td>
</tr>
<tr>
<td>Xenobiotics</td>
<td>Mercury, lead, arsenic, tin, thallium</td>
</tr>
<tr>
<td>Dietary/Endogenous</td>
<td>Dopamine, Epinephrine, Norepinephrine, Histamine</td>
</tr>
<tr>
<td>Nutrients required</td>
<td>SAMe (400-1600mg), Methionine (adult 13mg/kg), Choline (1.3-5gm), B12 (300-800mcg)</td>
</tr>
</tbody>
</table>

Osiecki, 2006; Mahan & Escott-Stump, 2008; Bryant & Knights, 2011
# Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Sulphation</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug metabolized eg.</strong></td>
<td></td>
</tr>
<tr>
<td>Salbutamol</td>
<td>Minoxidil</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Phenylephrine</td>
</tr>
<tr>
<td><strong>Xenobiotics</strong></td>
<td></td>
</tr>
<tr>
<td>Amines &amp; hydroxylamines</td>
<td>Terpenes</td>
</tr>
<tr>
<td>Phenols &amp; pentachbrophenol</td>
<td></td>
</tr>
<tr>
<td><strong>Dietary/Endogenous</strong></td>
<td></td>
</tr>
<tr>
<td>DHEA, melatonin,</td>
<td>Estrogen, Testosterone,</td>
</tr>
<tr>
<td>Catecholamines</td>
<td>Cortisol</td>
</tr>
<tr>
<td>Bile Acids, CCK</td>
<td>25 Hydroxyl Vit D</td>
</tr>
<tr>
<td>Tyramine</td>
<td>Ethyl Alcohol</td>
</tr>
<tr>
<td><strong>Nutrients required</strong></td>
<td></td>
</tr>
<tr>
<td>Cysteine (200-500mg)</td>
<td>Vitamin B6 (10-150mg)</td>
</tr>
<tr>
<td>Glutathione (100-500mg)</td>
<td>Molybdenum 100-500mcg</td>
</tr>
<tr>
<td>Methionine (adult 13mg/kg)</td>
<td></td>
</tr>
</tbody>
</table>

(Osiecki, 2006; Bryant & Knights, 2007; Sarris & Wardle, 2010)
## Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Acetylation</th>
<th>Drug metabolized eg.</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clonazepam</td>
<td>Sulfonamides,</td>
</tr>
<tr>
<td></td>
<td>Hydralazine, Procainamide</td>
<td>Dapsone, Isoniazid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Promizole,</td>
</tr>
<tr>
<td>Xenobiotics</td>
<td>2 Aminofluorine</td>
<td>Anilines</td>
</tr>
<tr>
<td>Dietary/Endogenous</td>
<td>Serotonin</td>
<td>Tyramine, Histamine,</td>
</tr>
<tr>
<td></td>
<td>PABA, Choline</td>
<td>Tryptamine,</td>
</tr>
<tr>
<td></td>
<td>Caffeine</td>
<td></td>
</tr>
<tr>
<td>Nutrients required</td>
<td>Vitamin B1 (5-150mg)</td>
<td>Vitamin B5 (20-200mg)</td>
</tr>
<tr>
<td></td>
<td>Vitamin B2 (10-40mg)</td>
<td>Lipoic Acid (100-500mg)</td>
</tr>
<tr>
<td></td>
<td>Vitamin B3 (11mg-50mg)</td>
<td>Vitamin C (250mg – 1gm)</td>
</tr>
</tbody>
</table>

(Osiecki, 2006; Bullock & Manias, 2007; Sarris & Wardle, 2010)
Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Glucuronidation</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug metabolized eg.</strong></td>
<td><strong>Drug metabolized eg.</strong></td>
</tr>
<tr>
<td>Salicylates, Naproxen, Steroids</td>
<td>Valproic Acid, Oxazepam, Lorazepam</td>
</tr>
<tr>
<td>Morphine, Benzodiazepines</td>
<td>Ciramidol</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Propranolol</td>
</tr>
<tr>
<td><strong>Xenobiotics</strong></td>
<td><strong>Phenols &amp; Thiophenols</strong></td>
</tr>
<tr>
<td><strong>Dietary/ Endogenous</strong></td>
<td><strong>Aniline, Butanol</strong></td>
</tr>
<tr>
<td>Bilirubin &amp; bile acids</td>
<td><strong>Estrogen, steroid hormones, Melatonin</strong></td>
</tr>
<tr>
<td>Vitamins A, D, E, K</td>
<td></td>
</tr>
<tr>
<td><strong>Nutrients required</strong></td>
<td><strong>Glutamine (0.5-3gm)</strong></td>
</tr>
<tr>
<td></td>
<td>aspartic acid (1.5-2gm), Iron (15-50mg)</td>
</tr>
</tbody>
</table>
| (Osiecki, 2006; Bryant & Knights, 2007; Sarris & Wardle, 2010)
Amino Acid Conjugation

Several amino acids are involved within the conjugation of the following intermediate metabolites:

- Glycine (most important)
- Taurine
- Glutamine
- Arginine
- Ornithine
## Liver Detoxification Pathways

<table>
<thead>
<tr>
<th>Amino Acid Conjugation</th>
<th>Adult dosages (SR daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug metabolized eg.</strong></td>
<td>Glycine: Salicylates, Chlorpheniramine, Brompheniramine</td>
</tr>
<tr>
<td><strong>Xenobiotics</strong></td>
<td>Glycine: Benzoic Acid Phenylacetic Acid, nepthylacetic Acid,</td>
</tr>
<tr>
<td><strong>Dietary/Endogenous</strong></td>
<td>Bile Acids, Cinnamics Acid, plant acids PABA</td>
</tr>
<tr>
<td><strong>Nutrients required</strong></td>
<td>Glycine (4-30gms) Taurine (250mg-2gms) Glutamine (500mg – 5gms)</td>
</tr>
</tbody>
</table>

Osiecki, 2006; Mahan & Escott-Stump, 2008; Bryant & Kknights, 2011)
Alcoholic Liver Disease
ALD

Features:

- Common cause of liver disease in western countries
- Reports in the US in 2009 suggested as many of 40% deaths from liver cirrhosis were attributed to alcohol (Mahan & Raymond, 2017)
- Some people are more predisposed to the damaging affects of alcohol – women, exposure to other drugs, genetic polymorphisms of alcohol metabolising enzymes, infections of liver, obesity, poor nutrition status (Mahan & Raymond, 2017, p564).
Alcoholic Liver Disease

Alcohol Misuse

- High levels of alcohol consumption are associated with social, psychological and physical problems
  (Walker, Colledge, Ralston & Penman, 2014; Bryant & Knights, 2011)

- Alcohol causes motility changes in the GIT, and affects the digestion and absorption of nutrients.

- Diarrhoea & weight loss frequently occur in alcoholics
  (Australian Government, 2004)

- Alcohol rehabilitation programs (AA) need to be recommended.
Alcoholic Liver Disease

Signs of Alcohol Misuse

- Narrowing of the drinking repertoire
- Priority of drinking over other activities
- Tolerance of effects of alcohol
- Repeated withdrawal symptoms
- Relief of withdrawal symptoms by further drinking
- Subjective compulsion to drink
- Reinstatement of drinking behaviour after abstinence

(Australian Government, 2004)
Alcoholic Liver Disease

Signs of Intoxication

- Drowsiness
- Errors of commission
- Disinhibition
- Dysarthria
- Ataxia
- Nystagmus
- Oedema (Ascites)

(Australian Government, 2004)
Alcoholic Liver Disease

- Alcoholics have demonstrated a difficulty with the breakdown of Acetaldehyde to Acetate when compared with normal subject or controls. The result of this malfunction results in raised brain concentration of acetaldehyde (Osiecki, 2006)
Alcoholic Liver Disease

Alcohol Withdrawal
Symptoms usually occur 1-3 days after the last drink
- Autonomic hyperactivity: visual hallucinations, mental confusion, tremor, agitation, elevated blood pressure, cardiovascular symptoms, diaphoresis.
- Dehydration
- Electrolyte disturbance
- Seizure

(Australian Government, 2004)
Alcoholic Liver Disease

Alcohol Detoxification

- Alcohol addiction is thought to be associated with the stimulation of endorphin receptors.
- This arises from alcohol being metabolized into acetaldehyde and the stimulation of dopamine production within the brain

(Bryant & Knights, 2007; Osiecki, 2006)
Alcoholic Liver Disease

Alcoholic Fatty Liver

- High or consistent serum ethanol is metabolized in the liver with a subsequent imbalance in the NADH/NAD ratio. This results in increased hepatic fatty acid synthesis with decreased fatty acid oxidation = fatty accumulation.
- This also impairs carbohydrate and protein metabolism
- Fatty deposits disappear with alcohol cessation
- Scar tissue of collagen can be formed which leads to cirrhosis

(Kumar & Clark, 2005, p. 389)
Alcoholic Liver Disease

Alcoholic Hepatitis

- When fatty deposits present in the liver, this can stimulate the influx of leucocytes and hepatic necrosis can ensue.
- If alcohol consumption continues, alcoholic hepatitis can progress to cirrhosis.
- May present with symptoms of ill health, mild jaundice to severe illness (high fever), jaundice, ascites, hepatomegaly and oedema.

(Kumar & Clark, 2005, p. 389)
Alcoholic Liver Disease

Alcoholic Cirrhosis

- Final stage of liver disease from alcohol abuse.
- Necrosis of liver cells causes high levels of inflammation, followed by fibrosis and nodule formation.
- Subsequent loss of function and altered blood flow.
- Alcohol is the most common cause of liver cirrhosis.

(Kumar & Clark, 2005, p. 389)
Alcoholic Liver Disease

Investigations

- Serum: checking albumin (below 28g/L) & prothrombin times that are prolonged indicate cirrhosis. Low sodium is indicative of severe liver disease.
- Liver Function Test (LFT): usual elevation in ALP and serum aminotransferase.
- Mean cell volume (MCV) or gamma-glutamyl transferase (GGT) is raised in approximately 50% of problem drinkers. MCV and GGT are useful for monitoring treatment response in individual cases where their values were elevated originally (Walker et al. 2014; Kumar & Clark, 2008)
Alcoholic Liver Disease

Investigations

- Ultrasound, CT or MRI scan: can identify fatty deposits and fibrosis, hepatomegaly, presence of surface nodules or changes to the vascularity
- Liver biopsy: confirms the type and severity of liver disease

(Kumar & Clark, 2005, p. 389)
Condition management

Important therapeutic considerations:
- Defective hepatic detoxification and metabolism deficits e.g. blood clotting, nutrient storage, metabolism, transport etc.
- Steatosis with or without fibrosis
- Alcoholic hepatitis
- Cirrhosis and hepatocellular carcinoma
- Muscle wasting and weight loss
- Maldigestion and malabsorption – pancreatic and bile insufficiency
- Portal hypertension
- Hypermetabolic state
- Severe micronutrient and macronutrient deficiencies – B vitamins, Vitamin A, digestive microbiome, protein
Therapeutic Considerations

- Alcohol rehabilitation programs – AA, counselling etc.
- Damaged oral, oesophageal, gut mucosa
  - Limit steatohepatitis by maintain intestinal homeostasis
- Dysbiosis
- Protein-energy malnutrition and widespread micronutrient deficiencies
- Insulin resistance
- Impaired protein synthesis – due to cytokine induced inflammation
- Addiction/dependence – emotional considerations
- Cognitive impact
- Other considerations – cardiac, renal
Therapeutic Actions

- A therapeutic action must describe both what changes (the aims of treatment) and what strategies are likely to be useful in facilitating those changes (recommendations).
- The plural ‘actions’ may be more apt in holistic practice as typically one treatment aim and one recommendation will address multiple health outcomes e.g. Glutamine
  - Support repair of intestinal epithelial cells
  - Raise hepatic antioxidant status
  - Energy source for intestinal cells facilitate epithelial regeneration
  - Substrate for glutathione synthesis – antioxidants rapidly depleted in gut inflammation
  - Supports phase II liver detoxification
Therapeutic Actions

- The therapeutic actions for the condition/disease must be determined before dietary, lifestyle and supplement recommendations are made.
- These are determined through biomedical and holistic assessment of the case, condition or disease.
- The aim is to provide effective, safe and reliable recommendations according to the level of patient self-efficacy.
- **Therefore we must:**
  - Appraise the evidence
  - Apply sound and realistic clinical reasoning
  - Determine the dosage
  - Review any potential drug/nutrient interactions
Treatment Aims
Therapeutic Actions

1. Eliminate hepatotoxic substances – referral for counselling
2. Correct protein energy malnutrition is prevalent to 20-60% cases – 1-1.5/kg/body weight
3. Screen for micronutrient deficiencies and supplementation as warranted
4. Raise nutritional status
5. Reduce liver inflammation
6. Restore intestinal epithelial surfaces
7. Correct dysbiosis
8. Stabilise blood glucose levels

(Rossia, Contea & Massironi, 2015)
Alcoholic Liver Disease

Nutritional Treatment

*Eliminate hepatotoxic substances*

- Avoid aspirin, NSAIDs, paracetamol and alcohol
- Fatty liver – abstinence until all tests return to normal. Small amounts can be consumed infrequently.
- Alcoholic hepatitis & cirrhosis – abstinence for life. Progression of the disease can be halted by correction of the underlying cause, namely alcohol use.
- Abstinence results in a positive prognosis (5 year survival is 35% - 60% with alcohol & 90% with abstinence).

(Kumar & Clark, 2005, p. 389)
Alcoholic Liver Disease

Nutritional Treatment

- A well balanced diet that is high in dietary protein (unless advanced liver disease)
- Five to six meals throughout the day
- Decrease consumption of any foods that may generate intolerance
  - Elimination diet
  - Allergy testing
- Maintain an adequate supply of nutrients that are required for liver clearance and support.

(Osiecki, 2006)
Alcoholic Liver Disease

Lifestyle Considerations

- Exercise 5-7 times/week, for 20-30 minutes at an intensity sufficient to raise the heart rate to 60-80% of maximum for the age group.
- Counselling
- Consider nutritional treatments for anxiety and depression, as these are often linked to alcohol abuse
  
  (Sarris & Wardle, 2010)
Alcoholic Liver Disease

*Nutrients most frequently deficient*
- Folate approximately 80% cases
- Vitamin B1, B3, B6, B12 and ADEK
- Zinc, Magnesium, Calcium
- Vitamin A – lower hepatic Vit A is found in alcoholics - alcohol acts as a competitive inhibitor of vitamin A oxidation to retinoic acid involving alcohol dehydrogenases and acetaldehyde dehydrogenases and alcohol disturbs retinoid homoeostasis (Wang, 2005).

*Vitamin B1, Vitamin B3 & Zinc*
- Alcohol reduces the absorption of B vitamins - B1 & B3.
- Vitamin B3 and Zinc can help metabolize alcohol and acetaldehyde thereby reducing the cravings for alcohol (Osiecki, 2006)
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dosage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>Start 50mg daily, divided dosages if not well tolerated, maintenance dose 25mg. Can start at 100mg if severely deficient. Zn test prior.</td>
<td>Low levels of zinc are associated with impaired alcohol metabolism, increased risk of cirrhosis and other complications of alcohol abuse. Zinc supplementation, when combined with ascorbic acid, greatly increases alcohol detoxification. (Pizzorno &amp; Murray, 2000, p. 1061-2) Vitamin B3 and Zinc can help metabolize alcohol and acetaldehyde thereby reducing the cravings for alcohol (Osiecki, 2006)</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>500-1000mcg</td>
<td>Alcoholism presents with reduced folic acid intake, abnormal metabolism and raised serum homocysteine levels. Activated folate (5-methyltetrahydrofolate) is crucial for hepatocyte synthesis, as it is required for purine and pyrimidine synthesis (Mahan &amp; Escott-Stump, 2008) Folate deficiency contributes significantly to mucosal changes and steatorrhea (Shils et al 2006, p1524-1525).</td>
</tr>
<tr>
<td>Vitamin A (retinol)</td>
<td>5000-10,000iu (up to 20,000iu), 2500 iu to 5000iu maintenance dose</td>
<td>Repairs epithelial cells Impaired retinoid synthesis occurs ALD Anti-inflammatory protection. Supports glutathione synthesis and regeneration</td>
</tr>
<tr>
<td><strong>ALD – Nutrients.</strong></td>
<td></td>
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<tr>
<td>---------------------</td>
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<td></td>
</tr>
<tr>
<td><strong>Beta-carotene</strong></td>
<td>15-30mg</td>
<td>Alcohol alters beta carotene conversion, increase toxicity and exacerbate hepatotoxicity (Stargrove et.al. 2008)</td>
</tr>
<tr>
<td><strong>Vitamin C</strong></td>
<td>Commence 500 to 1000mg TDS, maintenance dose 1000mg divided doses.</td>
<td>Daily supplementation (175 - 500mg) of ascorbic acid may be required for months to restore plasma and urinary ascorbate to normal levels post chronic alcohol abuse. Ascorbic acid helps ameliorate the effects of acute and chronic ethanol toxicity.</td>
</tr>
<tr>
<td><strong>B12</strong></td>
<td>500-2,000mcg</td>
<td>Vitamin B12 absorption is diminished with excessive alcohol consumption. Dose – 500-2,000mcg (Stargrove et.al. 2008)</td>
</tr>
<tr>
<td></td>
<td>50-200mg</td>
<td>B1, B3 - Alcohol reduces the absorption of B vitamin</td>
</tr>
<tr>
<td></td>
<td>100-200mg</td>
<td>Vitamin B12 absorption is diminished with excessive alcohol consumption (Stargrove et.al. 2008)</td>
</tr>
<tr>
<td></td>
<td>50-200mg</td>
<td>B12</td>
</tr>
<tr>
<td></td>
<td>500-2,000mcg</td>
<td>B12</td>
</tr>
</tbody>
</table>
Alcoholic Liver Disease

Further Nutrient Considerations:-

Antioxidants

- Antioxidant administration, either prior to or simultaneous with ethanol intake, inhibits lipoperoxidase formation and prevents fatty infiltration of the liver
  (Pizzorno & Murray 1999, p1061-1062; Shils et al. 2006, p1528)

Turmeric

- Found to reduce alcohol-induced inflammation
  (Stargrove et al. 2008)
Alcoholic Liver Disease

Further Nutrient Considerations Cont.

Mineral Levels

Calcium, Magnesium, Phosphorous, & Vitamin D

- Alcoholics have illnesses related to abnormalities of calcium, phosphorous, & vitamin D homeostasis. They have decreased bone density & bone mass, increased susceptibility to fractures & increased osteonecrosis

  - (Shils et al. 2006, p1528)

- Alcohol causes an increase in urinary magnesium & calcium losses. Magnesium is commonly deficient in alcoholics.

  - (Braun & Cohen, 2010; Stargrove et.al. 2008)

- Vitamin K - may arise when fat absorption is interrupted by pancreatic insufficiency, biliary obstruction, or intestinal mucosal abnormality secondary (secondary to folic acid deficiency).

  - (Shils et al. 2006, p1530)
Alcoholic Liver Disease

Further Nutrient Considerations Cont.

Essential Fatty Acids
- Ethanol has been shown to interfere with essential fatty acid metabolism, and as a result may produce symptoms of EFA deficiency if consumed in excess

Probiotics
- Probiotics may be useful, as the intestinal micro flora is severely altered in alcoholics
Alcoholic Liver Disease

Further Nutrient Considerations Cont.

**Glutamine** may reduce voluntary alcohol consumption, and aid with reducing inflammation of the gut mucosa
- Glutamine is useful in relieving alcohol intoxication (Braun & Cohen, 2010; Bryant & Knights, 2011)

**Phenylalanine**
- Phenylalanine is thought to inhibit enkephalinase and thereby maintain the brain's endogenous supply of opiate substances. Aids in alcohol detoxification & withdrawal (Osiecki, 2006)
Alcoholic Liver Disease – additional nutrients for consideration

<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>Anti-Oxidant</td>
</tr>
<tr>
<td>Carnitine</td>
<td>400-2000mg</td>
<td>Lipotropic, Reverses alcohol induced fatty livers.</td>
</tr>
<tr>
<td>Glutamine</td>
<td>500-3000mg</td>
<td>Withdrawals</td>
</tr>
<tr>
<td>Taurine</td>
<td>250-2000mg</td>
<td>Liver Detox</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>300-4000mg</td>
<td>Mood Elevation</td>
</tr>
<tr>
<td>N-acetylcyesteine</td>
<td>1.2-4gm</td>
<td>Enhance glutathione synthesis</td>
</tr>
<tr>
<td>Glutathione</td>
<td>100-500mg</td>
<td>Liver Detox</td>
</tr>
<tr>
<td>EPA</td>
<td>+500mg</td>
<td>Membrane Stability</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>200-800mg</td>
<td>Anti-oxidant + M.S.</td>
</tr>
<tr>
<td>Magnesium</td>
<td>400-800mg</td>
<td>Normal cellular metabolism and supports Phase I and II detoxification.</td>
</tr>
</tbody>
</table>

(Therapondos, Delahooke, & Hayes, 1999; Osiecki, 2006)
## Alcoholic Liver Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aldehyde Dehydrogenase Inhibitor:</strong> (Disulfiram)</td>
<td>Inhibits aldehyde dehydrogenase = raised acetaldehyde in serum when small amounts of alcohol are consumed. Symptoms = severe vasodilation, headache, shortness of breath, nausea, vomiting, dizziness, confusion &amp; chest pains. These effects can last for several hours.</td>
<td>Outside of the ‘clinical effects’ listed above there have been a number of cases of fatalities when combined with alcohol ingestion. Linked to hepatitis, blood &amp; blood vessel disorders.</td>
<td><em>Ascorbic acid, L-cysteine, Vitamin B1: Concurrent use reduces drug adverse effects of acetaldehyde toxicity, neurotoxicity &amp; aid liver cell maintenance</em></td>
</tr>
</tbody>
</table>
# Alcoholic Liver Disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acamprosate</td>
<td>Agonist effect on GABA receptors, resensitizing them to the presence of GABA while reducing glutamate surges. Reduces the symptoms of alcohol withdrawal</td>
<td>Gastro-intestinal irritation – diarrhoea, nausea, vomiting Skin rashes Generally well tolerated</td>
<td>None listed</td>
</tr>
<tr>
<td>Opioid Antagonist:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Reduces the cravings for alcohol and alters the euphoric effect when alcohol is consumed.</td>
<td>Transient post therapy symptoms include fatigue, insomnia, headache, dizziness &amp; nausea. Rarely hepatotoxicity can occur.</td>
<td>None listed</td>
</tr>
</tbody>
</table>

(Bullock et.al. 2007; Bryant & Knights, 2011)
# Alcoholic Liver Disease

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
</table>
| **Dopamine Receptor**     | **Antagonize dopamine D2 receptors = dopamine levels increase**<br>This reduces alcohol cravings. | **Extrapyramidal effects: sedation, alteration to the CNS regulation of motor coordination.** | **Co-enzyme Q10:** drug inhibits CoQ10 containing enzymes = cardiac depressant effects.  
**Phenylalanine:** Exacerbate tardive dyskinesia symptoms. Avoid.  
**Potassium:** together reduces the ventricular arrhythmia (SE of Thioridazine alcohol withdrawal)  
**Vitamin A:** elevated levels present with drug use. Avoid supplementation  
**Vitamin B3:** stimulates GABA receptors without attaching enhancing anti-craving effect.  
**Vitamin D:** CYP2D6 inhibitor = reduces the metabolism & breakdown of the drug. Avoid |

(Harkness & Bratmann, 2003; Bullock et.al. 2007; Stargrove et.al. 2008; Bryant & Knights, 2011)
Dietary & Nutritional Prescriptions

Cirrhosis and Hepatic Encephalopathy

- Moderate fat consumption (30% of total energy requirements). Reduce if steatorrhoea presents.
- Protein requirement is around 0.8-1.5gm/kg/day unless hepatic encephalopathy presents.
  - Protein needs to be limited to 60gm day with greater emphasis on BCAA and reduced AAA. Vegetable proteins need to be encouraged. (Moore, 2009, p329-330)
- Protein, methionine & choline deficiencies are implicated in the presentation of fatty liver, cirrhosis and hepatitis. (Shils et al. 2006, p. 1241)
Dietary & Nutritional Prescriptions

Cirrhosis and Hepatic Encephalopathy

- High energy diet (20-40 kcal/kg/day) with a higher emphasis on complex carbohydrates.
  - Inclusion of complex carbohydrates may reduce insulin requirements as insulin resistance commonly presents.
    (Shils et al. 2006, p. 1241)
- Long-term management would include a reduced fat diet (25-30% of total daily calories)
  (Mahan & Escott-Stump, 2008, p.729)
- Elimination of alcohol
- Small, frequent meals
  (Moore, 2009, p. 328-329)
Steatosis (Fatty Liver)

- Non-alcoholic steatohepatitis (NASH), the lynchpin between steatosis and cirrhosis in the spectrum of non-alcoholic fatty liver disorders (NAFLD). NAFLD is now present in 17% to 33% of Americans and parallels the frequency of central adiposity, obesity, insulin resistance, metabolic syndrome and type 2 diabetes. NASH could be present in one third of NAFLD cases.

- Pathogenic concepts for NAFLD/NASH must account for the strong links with over nutrition and underactivity, insulin resistance, and genetic factors. Lipotoxicity, oxidative stress, cytokines, and other proinflammatory mediators may each play a role in transition of steatosis to NASH (Farrell & Larter, 2006).
Steatosis (Fatty Liver)

- The present "gold standard" management of NASH is modest weight reduction, particularly correction of central obesity achieved by combining dietary measures with increased physical activity. Whether achieved by "lifestyle adjustment" or anti-obesity surgery, this improves insulin resistance and reverses steatosis, hepatocellular injury, inflammation, and fibrosis (Farell & Larter, 2006).

- **Nutrient specific**
  - Chromium and alpha lipoic acid
  - Fish oils
  - Carnitine and NAC
L-Carnitine Supplementation to Diet: A New Tool in Treatment of Nonalcoholic Steatohepatitis—A Randomized and Controlled Clinical Trial

Mariano Malaguarnera, AP¹, Maria Pia Gargante, MD¹, Cristina Russo, MD¹, Tijana Antic, MD¹, Marco Vacante, MD¹, Michele Malaguarnera, MD², Teresio Avitable³, Giovanni Li Volti, AP² and Fabio Galvano, AP²

OBJECTIVES: Nonalcoholic steatohepatitis (NASH) is a known metabolic disorder of the liver. No treatment has been conclusively shown to improve NASH or prevent disease progression. The function of L-carnitine to modulate lipid profile, glucose metabolism, oxidative stress, and inflammatory responses has been shown. The aim of this study was to evaluate the effects of L-carnitine's supplementation on regression of NASH.

METHODS: In patients with NASH and control subjects, we randomly dispensed one 1-g L-carnitine tablet after breakfast plus diet and one 1 g tablet after dinner plus diet for 24 weeks or diet alone at the same dosage and regimen. We evaluated liver enzymes, lipid profile, fasting plasma glucose, C-reactive protein (CRP), tumor necrosis factor (TNF)-α, homeostasis model assessment (HOMA)-IR, body mass index, and histological scores.

RESULTS: At the end of the study, L-carnitine-treated patients showed significant improvements in the following parameters: aspartate aminotransferase ($P=0.000$), alanine aminotransferase (ALT) ($P=0.000$), γ-glutamyl-transpeptidase (γ-GT) ($P=0.000$), total cholesterol ($P=0.000$), low-density lipoprotein (LDL) ($P=0.000$), high-density lipoprotein (HDL) ($P=0.000$), triglycerides ($P=0.000$), glucose ($P=0.000$), HOMA-IR ($P=0.000$), CRP ($P=0.000$), TNF-α ($P=0.000$), and histological scores ($P=0.000$).

CONCLUSIONS: L-carnitine supplementation to diet is useful for reducing TNF-α and CRP, and for improving liver function, glucose plasma level, lipid profile, HOMA-IR, and histological manifestations of NASH.

Source: Malaguarnera M et al 2010
N-Acetylcysteine Improves Liver Function in Patients with Non-Alcoholic Fatty Liver Disease

**Background and Aims:** Non-alcoholic fatty liver change is a common disease of the liver in which oxidative stress plays a basic role. Studies are largely focused on protecting the liver by means of anti-oxidative material. The aim of this study is to evaluate the role of N-acetylcysteine in the process of liver injury.

**Methods:** Thirty patients with non-alcoholic fatty liver steatosis were randomly selected to receive either N-acetylcysteine or vitamin C. Liver function tests (alanine aminotransfrase, aspartate aminotransfrase and alkaline phosphatase) were measured as well as the grade of steatosis, the pattern of its echogenicity, the span of the liver and the spleen and the portal vein diameter before the intervention. Patients were followed up using the same method of evaluation repeated in the first, second and third months.

**Results:** The mean age (SD) was 40.1(12.4) in patients receiving NAC and 46(10.4) years in patients receiving vitamin C (P = 0.137). NAC resulted in a significant decrease of serum alanine aminotransfrase after three months, compared to vitamin C. This effect was independent of the grade of steatosis in the initial diagnosis. NAC was able to significantly decrease the span of the spleen.

**Conclusions:** N-acetylcysteine can improve liver function in patients with non-alcoholic fatty liver disease. Better results may be achievable in a longer follow up.

Mice study – Conclusion: L-carnitine, NAC and genistein showed a significant protective effects in liver fibrosis induced by carbon tetrachloride.

Protective effects of L-carnitine, N-acetylcysteine and genistein in an experimental model of liver fibrosis

Kaan Demiroren*, Yasar Dogan, Halil Kocamaz, Ibrahim Hanifi Ozercan, Selcuk Ilhan, Bilal Ustundag, Ibrahim Halil Bahcecioglu

Yuzuncu Yil University, Dursun Odabas Medical Center, Pediatric Gastroenterology, Van, Turkey

Clinics and Research in Hepatology and Gastroenterology (2013)

Summary

Aim: Liver fibrosis is a reversible wound-healing response that occurs following liver injury. In this study, we aimed to investigate the possible protective effects of L-carnitine, N-acetylcysteine and genistein in liver fibrosis induced by carbon tetrachloride (CCL4). In addition, the effects of these agents were compared in the same study.

Methods: In this study, rats were randomly allocated into 8 groups, consisting of 10 rats each, as follows: a control group, CCL4, L-carnitine, N-acetylcysteine, genistein, CCL4 and L-carnitine, CCL4 and N-acetylcysteine, and CCL4 and genistein. At the end of 6 weeks, blood and liver tissue specimens were collected. Alanine aminotransferase (ALT); aspartate aminotransferase (AST); complete blood count, tumor necrosis factor-α (TNF-α); platelet-derived growth factor-BB (PDGF-BB); interleukin-6 (IL-6); liver glutathione level; oxidant/antioxidant status; scores of hepatic steatosis, necrosis, inflammation, and fibrosis; and the expression of α-smooth muscle actin were studied.

Results: Although the ALT and AST values in the group administered CCL4 were significantly higher than in all the other groups (P<0.05), there was no significant difference between the control group and the groups administered CCL4 combined with L-carnitine, N-acetylcysteine and genistein (P>0.05). There were significant differences in the levels of TNF-α, PDGF BB and IL-6 (P<0.05) between the CCL4 group and the groups with L-carnitine, N-acetylcysteine and genistein added to CCL4. N-acetylcysteine and genistein had positive effects on the oxidant/antioxidant status and on liver necrosis and fibrosis scores.

Conclusions: In our study, L-carnitine, N-acetylcysteine and genistein showed significant protective effects in liver fibrosis induced by CCL4.
Hepatitis A

- Hepatic viral infection spread through the faecal-oral route or when infected faecal matter enters the mouth.
- Symptoms can be debilitating but most people infected with hepatitis A recover completely.
- Hepatitis A is an acute (short-term but quite severe) infection of the liver caused by the hepatitis A virus.
- Infants and young children infected with hepatitis A will rarely show symptoms of infection and may appear quite well, or have only mild symptoms. The majority of adults will show symptoms (Hepatitis Australia)
Symptoms of Hepatitis A

- Symptoms of hepatitis A include:
  - fever;
  - weakness;
  - fatigue;
  - loss of appetite;
  - nausea;
  - joint aches and pains;
  - vomiting; and jaundice (yellowish eyes and skin, dark urine and pale-coloured faeces).
Testing for Hepatitis A

○ The incubation period varies between 15 and 50 days, average of 30 days. HAV is excreted for up to two weeks before the onset of symptoms. Therefore, people should be considered infectious for a week after the onset of jaundice.

○ The detection of IgM hepatitis A antibodies (anti-HAV IgM) confirms recent infection. The detection of IgG hepatitis A antibodies (anti-HAV IgG) indicates past infection and immunity against hepatitis A infection.

○ Liver function test (LFTs) abnormalities, specifically elevated serum bilirubin and serum aminotransferase (ALT and AST) values, may also indicate acute infection (Hepatitis Australia)
Hepatitis B

- Hepatitis B is the most common liver infection in the world.
- Blood-borne virus that attaches to healthy liver cells and multiplies. This replication of the virus then triggers an immune response. People are often unaware they have been infected with the hepatitis B at this stage.
- If undiagnosed and not managed Hepatitis B infection can lead to cirrhosis (scarring of the liver), liver cancer or liver failure.
- In Australia, it is estimated that 225,000 people are chronically infected with hepatitis B (MacLachlan, J.H., et al. 2011; Aust N Z J Public Health, 2013). However, nearly half of those living with chronic hepatitis B in Australia are undiagnosed (Hepatitis Australia)
Hepatitis B

- Hepatitis B infection is considered to be ‘acute’ during the first 6 months after infection. If hepatitis B virus tests (HBsAg+) are positive after 6 months, then a person is considered to have ‘chronic’ (long term) hepatitis B infection which can last a lifetime.

- Annual liver check-ups are essential

(Hepatitis Australia)
Hepatitis C

- The hepatitis C virus is a member of the flavivirus family of ribonucleic acid (RNA) viruses. The virus reproduces by making many copies of itself in liver cells.
- The hepatitis C virus does not kill liver cells directly, but the immune response initiated by the presence of the virus in the liver can cause liver inflammation and cell death.
- There are six main genotypes (strains) of hepatitis C. Each genotype contains numerous subtypes, labelled a, b, or c. Genotypes 1a and 1b (54% prevalence) and 3a (37% prevalence) are the most common genotypes in Australia (Hepatitis Australia)
Hepatitis C

- It is estimated that 150 million people worldwide are chronically infected with hepatitis C.
- In Australia, it is estimated that approximately 233,000 are living with chronic hepatitis C.
- The estimated number of new cases diagnosed of hepatitis C infection has declined from 16,000 in 2001 to 10,261 in 2011. The majority of these had hepatitis C for some time (Hepatitis Australia)
Hepatitis C

- In 2011, 60% of newly acquired hepatitis C infections (within that last two year) were identified as having resulted from unsafe injecting drug use. The remaining people with hepatitis C were infected in other ways, including:
  - unsterile tattooing or body piercing procedures
  - unsterile medical procedures or vaccinations (particularly in countries with high rates of hepatitis C)
  - needle-stick injuries and accidental exposure to infected blood or blood products
  - exposure to blood in the home
  - some other form of blood-to-blood contact.
  - Some people with hepatitis C cannot identify how they were infected.

(Hepatitis Australia)
Treatment Aims and Hepatitis Management

- Reduce/minimal liver toxins – alcohol, paracetamol, chemicals, tobacco, OTC anti-histamines etc.
- Prescribe anti-inflammatory diet, high plant based diet, with minimal saturated fats from animal proteins; although need to ensure adequate daily protein is attained. Low GI/GL diet, therefore reduce refined sugars, carbohydrates and avoid high-fructose corn syrup.
- Nutritional support
  - Antivirals
  - Anti-inflammatory
  - Hepatoprotective and restoratives
  - Antioxidants – especially restoration of glutathione
  - Support energy metabolism and nervous system (mood)
Fat-Restricted Diet

- **Food Allowed**
  - **Cheese**
    - Cottage cheese 1/4c to be used as substitute for 1oz of cheese, or low fat cheeses containing less than 5% butterfat.
  - **Eggs**
    - Three per week prepared only with fat from fat allowance; egg whites as desired; low-fat egg substitutes.
  - **Fats**
    - Choose up to the limit allowed among the following
      - 1 tsp butter or margarine
      - 1 tsp mayonnaise
      - 1 strip crisp bacon
      - 6 small nuts
      - 5 small olives
    - This is an example diet of what is offered through many services working in this area!

- **Food Excluded**
  - Whole milk, buttermilk (from whole milk), chocolate milk, cream
  - More than one/day unless substituted for part of the meat allowed
  - Any in excess of amount prescribed on diet: all others
**Hepatitis - Nutrients**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage</th>
<th>Description</th>
</tr>
</thead>
</table>
| Zinc             | Start low if nausea a factor, otherwise 25-50mg daily | Raise CuZnSOD  
Reduces serum ferritin reducing oxidation  
(Hechtman, 2014) |
| Vitamin C        | 500mg divided dosages up to 4000mg  | Antiviral effect through increased production of interferon IFN-α/β.  
(Hechtman, 2014) |
| N-acetyl Cysteine| 1800mg                              | Regenerate glutathione and support phase I & II detoxification  
Antioxidant  
(Hechtman, 2014) |
| Selenium         | 25-250mcg                           | Antioxidant and raise glutathione  
Good in combination with NAC  
(Hechtman, 2014) |
| Glutamine        | 500-3,000mg                         | Liver disease and cirrhosis are associated with depletion of endogenous Glutathione.  
Support detoxification  
Liver hepatic cellular regeneration |
### Hepatitis – Nutrients Cont.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dosage</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha-lipoic Acid</strong></td>
<td>200-600mg</td>
<td>Antioxidant superoxide and hydrogen peroxide</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improve hepatic glucose metabolism (Hechtman, 2014)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mice study: alpha-lipoic acid (LA) improved liver anti-oxidative capacity by increasing total superoxide dismutase (tSOD), manganese SOD (MnSOD), and copper/zinc-SOD (Cu/ZnSOD) activity as well as glutathione (GSH) content. It can be concluded that LA ameliorates lipid peroxidation and nitrosative stress NAFLD through an increase in SOD activity and GSH level (Stankovic et al 2013, J Med Food 00 (0)1–8)</td>
</tr>
<tr>
<td><strong>Omega 3</strong></td>
<td>1000mg and DHA 1000mg/day</td>
<td>Anti-inflammatory (Hechtman, 2014)</td>
</tr>
</tbody>
</table>
| **Activated B Complex** | See individual doses per B vitamin | Energy metabolism  
Support hepatic detoxification and methylation pathways (Hechtman, 2014) |
Hepatitis C new drug treatment, available at:

- New generation direct-acting antiviral (DAA) medicines available on the PBS from 1 January 2017 for all people with HCV over 18 years of age:
  - Daklinza® (daclatasvir)
  - Harvoni® (sofosbuvir + ledipasvir)
  - Ibavyr® (ribavirin)
  - Sovaldi® (sofosbuvir)
  - Viekira Pak® (paritaprevir + ritonavir + ombitasvir + dasabuvir)
  - Viekira Pak RBV® (paritaprevir + ritonavir + ombitasvir + dasabuvir + ribavirin)
  - Zepatier® (grazoprevir + elbasvir)

- The medicines are better than the previous, i.e. interferon
  - Result in a cure for 90-95% of people taken as tablets, with very few side-effects taken for as little as 8-12 weeks in most cases,
Discussion
Case Study

58 year old male

Presenting symptoms

- Has just been diagnosed with the initial stages of cirrhosis of the liver.
- Eating fatty foods present with loose stool and mild digestive bloating
- He also presents with loss of appetite – this has been getting worse for the past 4 months
- Stools commonly loose & odorous. Undigested food present
- Sensitive to the smell of strong perfumes and household cleaners
Case Study

Medications / Supplements
Lipitor (statin): 20mg taken at night
Accupril (ACE Inhibitor): 10mg at night
Panadol: 2 tablets as required (usually 4-5x week)
Case Study

Family History
- Mother: hypertension, lung cancer (Dec. 56yo.)
- Father: osteoarthritis, diabetic (Dec. 58yo.)

Past Medical History
- **Infant:** unsure of delivery, vaccinated
- **Childhood:** broke arm when he was 6 falling off a wall, mumps at 8 years old
- **Adolescence:** dislocated knee playing football (17yo.) trouble with that knee ever since
Case Study

System Presentation


- **Immune**: wounds slow to heal (1-2 weeks)

- **Urinary**: stream is diminished. Has to get up 1-2 times to urinate. No pain. Erectile dysfunction present.

- **Circulatory**: blood pressure diagnosed 12 years prior. Varicose veins presenting around the navel. Easy bruising

- **Musculo-skeletal**: left knee aches with over use, there is not the full flexion or extension. No heat or swelling
Case Study

Physical Examination Results

- **Nails**: spooning, white spots on 8/10 fingers, red nail beds, cracking on the sides of the nails
- **Skin**: yellowish
- **Appearance**: central adiposity
- **Height**: 178cm  **Weight**: 67kg  **Waist**: Hip 0.85 (Male>0.95)  **Blood pressure**: 136/89
- **Tongue**: flabby, central crack, teeth indentations on periphery, quiver
- **Eyes**: pterygium in both eyes
- **Zinc tally**: no immediate taste
## Case Study

<table>
<thead>
<tr>
<th>Time</th>
<th>Daily Dietary Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>7am</td>
<td>Dry white toast 1 cup of black coffee</td>
</tr>
<tr>
<td>9.30am</td>
<td>1 cup of black coffee</td>
</tr>
<tr>
<td>1pm</td>
<td>Ham and cheese sandwich on brown bread</td>
</tr>
<tr>
<td>7 pm</td>
<td>Fish and salad: white fish with lettuce, tomato, onion, cucumber (no dressing) 3 glasses of wine</td>
</tr>
<tr>
<td></td>
<td>Water: 1.5 litres</td>
</tr>
</tbody>
</table>
Discussion

- Discuss 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 the contributing factors, predisposing and sustaining factors for this patient's case.

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


References


References


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