Proteins and Amino Acids

Naturopathic Nutrition 1
Learning Outcomes

On successful completion you will be able to:

• Outline the structure, functions, dietary sources and factors affecting the bioavailability of protein and amino acids and discuss their primary roles in metabolic physiological processes
Proteins - Structure

- Compounds containing C, H, O, N
- Building blocks - amino acids
Each amino acid contains:

- Amino group – NH₃
- Carboxylic acid group - COOH
- Unique side group which differentiates each amino acid - R group
- Approx. 1000 AAs in nature

(Lanham-New, Macdonald and Roche 2011)
Several amino acids and their derivatives are important in metabolism, but generally not associated with protein.

The human body commonly uses 20 amino acids for polypeptide synthesis—as building blocks of protein.

More than half of the amino acids are considered nonessential, i.e. the body can synthesise them.

There are nine amino acids that humans cannot synthesise either in sufficient quantities or at all, so they must be supplied with the diet; they are considered essential.

Sometimes nonessential amino acids can become essential under specific circumstances, i.e. conditionally essential.

(Liska ed. 2004)
# Proteins - Structure

<table>
<thead>
<tr>
<th>Some Non-Essential Amino Acids</th>
<th>Essential Amino Acids</th>
<th>Conditionally Essential Amino Acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>Histidine</td>
<td>Arginine</td>
</tr>
<tr>
<td>Aspargine</td>
<td>Isoleucine</td>
<td>Cysteine</td>
</tr>
<tr>
<td>Aspartic Acid</td>
<td>Leucine</td>
<td>Glutamine</td>
</tr>
<tr>
<td>Citrulline</td>
<td>Lysine</td>
<td>Glycine</td>
</tr>
<tr>
<td>Glutamic Acid</td>
<td>Methionine</td>
<td>Proline</td>
</tr>
<tr>
<td>Proline</td>
<td>Phenylalanine</td>
<td>Tyrosine</td>
</tr>
<tr>
<td>Serine</td>
<td>Threonine</td>
<td>Carnitine</td>
</tr>
<tr>
<td>Selenocysteine</td>
<td>Tryptophan</td>
<td>Taurine</td>
</tr>
<tr>
<td></td>
<td>Valine</td>
<td>Ornithine</td>
</tr>
</tbody>
</table>
Proteins - Structure

- **Dipeptide** - two amino acids
- **Tripeptide** - three amino acids
- **Oligopeptide** - several amino acids
- **Polypeptide** - from 50 amino acids
- **Proteins** - a few dozen to several hundred amino acids long
• **Protein denaturation** – occurs when proteins are subjected to heat, acid or other conditions that disturb their stability. This is accompanied by uncoiling of the protein/amino acid structure, loss of shape and loss of function, e.g. hardening of an egg when it is cooked.
Proteins - Functions

• The human body contains an estimated 10,000 to 50,000 different kinds of proteins

• Each protein has a specific function that is determined during protein synthesis

• In a normal weight person, protein accounts for about 17% of weight (12 kg in 70 kg man)
## Proteins - Functions

<table>
<thead>
<tr>
<th></th>
<th>Lean man 70 kg</th>
<th>Obese man 100 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>60%</td>
<td>47%</td>
</tr>
<tr>
<td>Protein</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>Fat</td>
<td>17%</td>
<td>35%</td>
</tr>
<tr>
<td>Remainder</td>
<td>6%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Proteins - Functions

1. As building materials for growth and maintenance

   - Building blocks of muscles, blood, skin, and most body structures. For example, to build bones, cells first lay a **matrix** from protein **collagen**, and then fill it with mineral crystals

   - Collagen provides building material for ligaments, tendons, artery walls, scars, etc.

   - Proteins are also needed for general replacement, e.g. of skin, muscle cells, or GI tract cells
2. As enzymes

- Enzymes break down, build anew and transform substances, without themselves being altered in the process.

- Enzymes can act as catalysts to change the rate of reactions occurring in the body.

Example: digestive enzymes.
3. As hormones

- Hormones can be derived from cholesterol, amino acids or polypeptides
- **Tyrosine** + Iodine $\rightarrow$ **thyroid hormones**
- **Tyrosine** $\rightarrow$ dopamine, norepinephrine, epinephrine
- **Tryptophan** $\rightarrow$ melatonin
- **Two polypeptide chains** *$\rightarrow$ insulin
- **One polypeptide chain** $\rightarrow$ glucagon, PTH, calcitonin
4. As immunoproteins (immunoglobulins, antibodies)

- Immunoproteins IgG, IgA, IgM, IgE, IgD are proteins that are found in blood or other bodily fluids

- They are used by the immune system to identify and neutralise foreign objects, such as bacteria and viruses
5. Transport proteins

- Proteins that combine with other substances in the blood or within cells to provide a mode of transport for those substances*
  - Albumin (Ca, Zn, vit B6)
  - Transthyretin+retinol binding protein (vitamin A)
  - Hemeproteins (O2)
  - Transferrin (Fe)
  - Ceruloplasmin (Cu)
6. As acid-base regulators

- Proteins have negative charges on their surfaces which attract hydrogen ions because they have positive charges.

- By accepting and releasing $H^+$ they maintain acid-base balance in body fluids.

- Proteins (-) attract Hydrogen (+)
Proteins - Functions

7. As regulators of fluid balance

- Proteins attract water
- If plasma proteins leak out of capillary walls faster than they can be reabsorbed, fluid accumulates in tissues → swelling, oedema
- Protein related causes of oedema:
  - Excessive protein losses due to kidney disease, large wounds
  - Inadequate protein synthesis caused by liver disease
  - Inadequate dietary intake of protein
8. Other roles - conjugated proteins

- Conjugated proteins are proteins joined to non-protein components

**Glycoproteins:** proteins bound to carbohydrates found in mucus, connective tissue (collagen, elastin, bone matrix)

The carbohydrate components - glucose, galactose, mannose, fructose, N-acetylglucosamine, etc.

**Proteoglycans** (a special class of glycoprotein): proteins bound to glycosaminoglycans

These make up the extracellular matrix that surrounds tissues and organs e.g. hyaluronic acid, chondroitin sulphate, keratin sulphate, etc.
Protein Synthesis (more details see Biochemistry Lecture)

- In response to stimuli/messages, cells synthesise proteins according to the genetic information provided by the DNA in the nucleus of each cell.
- DNA dictates the order in which amino acids must be linked together to form a given protein.
Protein Turnover and Amino Acid Pool

• Within each cell proteins are continually being made and broken down; a process known as protein turnover

• When proteins break down, they free amino acids to join the general circulation

• These amino acids + diet-derived amino acids = amino acid pool

• Amino acids taken in excess may be used to make fat when energy and protein intakes exceed need. The amino acids are deaminated; the nitrogen is excreted, and the remaining carbon fragments are converted to fat and stored for later use

(Rolfes et al 2006)
Proteins - Metabolism

Urea Cycle

KEY TO ENZYMES (Circled Numbers)
1. Carbamoyl-phosphate synthase (ammonia)
2. Ornithine carbamoyltransferase
3. Argininosuccinate synthase
4. Argininosuccinate lyase
5. Arginase
Dietary (Exogenous) Sources of Proteins

The diet is the primary source of all essential amino acids as well as any additional nitrogen needed for the synthesis of the nonessential amino acids and/or other nitrogen containing compounds.

These dietary sources include:

- animal products: meat, poultry, fish and dairy products (with the exception of butter, sour cream which are primarily composed of fat)
- plant products: grains, grain products, legumes, beans, nuts, seeds and vegetables
- with the exception of highly refined products like oils, alcohol, white sugar, vinegar, etc. all whole foods contain protein (even fruit)
Endogenous Sources of Proteins - Non-dietary source of amino acids and nitrogen

Including:

• Desquamated mucosal cells, which generate about 50 g of protein per day
• Digestive enzymes and glycoproteins, which generate about 17 g of protein a day
• These proteins are digested and the amino acids absorbed
• These may total about 70 g protein or more per day

(Geissler and Powers 2005)
Proteins - Metabolism

Regardless of their source, any of these amino acids can be used to:

- Make body proteins or other nitrogen-containing compounds
- If a particular nonessential AA is not available the body can make it from another = Transamination
- If an essential AA is missing, the body may break down some of its own protein to obtain it
- They can also be stripped of their nitrogen and used for energy (either immediately or stored as fat for later use*) = Deamination
Transamination of Amino Acids

• Transamination is an important step in the synthesis of some nonessential amino acids. The process is catalysed by enzymes that need B6 to function.
• The amino group of an amino acid is transferred onto an enzyme
• The enzyme then transfers the amino group on to an acceptor, (a keto acid)
• Thus forming the new amino acid
• This is a reversible reaction
• Remember this reaction is dependent on vitamin B6
Proteins - Metabolism

Using Amino Acids for Energy and Glucose

• When glucose and fatty acids are limited, cells are forced to use amino acids for energy and glucose

• The body does not store proteins as it does carbohydrates (glucose as glycogen) and fats (triglycerides in adipose tissue)

• Protein in the body is available as tissue components

• When the need arises, the body dismantles its tissue proteins and uses them for energy - over time energy deprivation causes lean tissue wasting
Deamination of Amino Acids

• When amino acids are broken down, they are stripped of their nitrogen-containing amino group which is converted to **ammonia**, which is then released into the bloodstream

• The liver converts toxic ammonia into a less toxic compound **urea** (urea cycle) and returns urea to the bloodstream

• The kidneys filter urea out of the blood → amino nitrogen ends in urine

• The remaining carbon fragments of amino acids may be used to produce glucose (**glucogenic amino acids**), ketones (**ketogenic amino acids**), cholesterol or fat
## Proteins - Sources

<table>
<thead>
<tr>
<th>Source</th>
<th>Protein (Grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheddar cheese, 28g / 1 oz.</td>
<td>7</td>
</tr>
<tr>
<td>Egg, 1 medium</td>
<td>6</td>
</tr>
<tr>
<td>Milk, skim, 1 cup</td>
<td>8</td>
</tr>
<tr>
<td>Yogurt, low-fat, plain, 1 cup</td>
<td>12</td>
</tr>
<tr>
<td>Chicken, light meat, roasted, no skin (4oz/100g)</td>
<td>31</td>
</tr>
<tr>
<td>Sirloin steak, choice cut, trimmed, grilled (4oz/100g)</td>
<td>35</td>
</tr>
<tr>
<td>Tuna, canned, in water (4oz/100g)</td>
<td>33</td>
</tr>
<tr>
<td>Oatmeal, 1 cup cooked</td>
<td>6</td>
</tr>
<tr>
<td>Rice, brown, 1 cup cooked</td>
<td>5</td>
</tr>
<tr>
<td>Whole wheat bread, 2 slices</td>
<td>6</td>
</tr>
<tr>
<td>Almonds, 1 oz. (20-25 shelled nuts)</td>
<td>6</td>
</tr>
<tr>
<td>Cashews, 1 oz. (16-18 nuts)</td>
<td>4</td>
</tr>
<tr>
<td>Lentils, ½ cup cooked</td>
<td>8</td>
</tr>
<tr>
<td>Peanut butter, 2 Tbsp.</td>
<td>10</td>
</tr>
<tr>
<td>Red kidney beans, ½ cup canned</td>
<td>8</td>
</tr>
<tr>
<td>Soybeans, ½ cup cooked</td>
<td>10</td>
</tr>
<tr>
<td>Tofu, 4 oz.</td>
<td>9</td>
</tr>
</tbody>
</table>

(USDA 2008)
Protein requirements are difficult to establish; none of the advances in biology provide a solution

- There are no unequivocal biochemical or physiological deficiency symptoms other than those of severe deficiency (growth failure, tissue wasting) → we can only identify levels below requirement

- All methods of determining protein requirements are imprecise

(Millward 2005)
Methods of Determining Protein Requirements:

Nitrogen balance:

- Demands are estimated from measurements of all losses of nitrogen in subjects adapted to diets with different levels of protein.
- They establish the amount of protein that must be fed to balance N losses and to establish nitrogen equilibrium.
- From these data protein requirements are: 0.66 g/kg body weight

(Millward 2005)
Nitrogen Balance

- In healthy adults protein synthesis balances with degradation
- Protein intake from foods balances with nitrogen excretion in the urine, faeces, and sweat
- Nitrogen intake = nitrogen output → **nitrogen equilibrium (zero nitrogen balance)**
- Nitrogen intake > nitrogen output → **positive nitrogen balance**; body synthesises more protein than it degrades - building and/or replacing tissue e.g. infants, children, pregnant women, people recovering from illness
- Nitrogen intake < nitrogen output → **negative nitrogen balance**; body degrades (uses up) more protein than it synthesises (starvation, burns, injuries, infections, fever)
Nitrogen balance potential problems:

- Essentially the method is imprecise
- Intake can be overestimated; loss underestimated
- Equilibrium can be influenced by intakes of other nutrients
- Adaptation can result over the long term (nitrogen balance studies are short-term)

(Millward 2005; Geissler and Powers 2005)
Protein Requirements/Bioavailability

- The RDA for protein incorporates a wide margin of safety - see next slide
- It is estimated that risk of protein deficiency would start at values between 0.4-0.5 g/kg of body weight
- However, diets providing as little protein as this are highly unlikely to be adequate in terms of energy or other nutrients
- Theoretically, it is impossible to become protein deficient if you are meeting your energy requirements with a varied diet of natural foods

(Rose 1975; Millward 2003; Geissler and Powers 2003)

Adults (including older adults) – 0.83 g per kg of body weight per day.

Infants, children and adolescents – between 0.83 g and 1.31 g per kg of body weight per day depending on age.

Pregnant women – additional intake of 1 g, 9 g and 28 g per day for the first, second and third trimesters respectively.

Breast-feeding women – additional intake of 19 g per day during the first 6 months of lactation and 13 g per day thereafter.
FOCUS: Protein Requirements for Athletes

Theoretically athletes may be considered to have a higher requirement for protein due to the increased catabolism of amino acids that occurs during exercise.

There are conflicting views on how this increased need should be met:

• Young (1986) suggests an increased consumption of protein – between 1.0-1.5 g of protein/kg body weight.

• Millward (1999) however states that the increased need for protein in athletes will automatically be met as a proportion of the increased calorie requirements which in his opinion may even take athletes over the safe upper limit of 1.5 g/kg.
FOCUS: Protein Requirements for Athletes

Conflicting views continued:

• The Institute of Medicine’s Food and Nutrition Board makes no extra allowance for physical work or training; the margin of safety is already included in the RDA

• American and Canadian Dietetic Associations: these groups propose an increased protein allowance for endurance athletes 1.2-1.4 g and resistance athletes 1.6-1.7 g of protein/kg body weight per day

(NRC 1989; ADA 2000)
FOCUS: Protein Requirements for Athletes

Textbook: Human Nutrition by Geissler and Powers (2005): *Protein requirements are generally not considered to vary with energy expenditure and protein requirements are usually provided by the increased food energy intakes."

Textbook: Understanding Normal and Clinical Nutrition by Rolfes et al (2005): *The protein RDA is the same for athletes as for others, although some fitness authorities recommend a slightly higher intake."
FOCUS: Protein Requirements for Athletes

**General Consensus:** Even the highest protein intake recommendations can be met through diet alone (even vegetarian diet), without the use of protein or amino acid supplements provided energy intake is adequate.

(Geissler and Powers 2005; Messina et al 2004; Rolfes et al 2006)

**Comment - Marion Nestle, Ph.D., Chair of the Department of Nutrition, New York University** - ‘We never talk about protein anymore, because it’s absolutely not an issue… getting enough is simply a matter of getting enough calories.’

(Weisenthal 1995)
Protein Quality: Two factors influence protein quality - protein digestibility and its amino acid composition

Digestibility: This depends on the source of protein and the other foods eaten with it

- The digestibility of most animal proteins is high (90-99%); plant proteins are less digestible (70-90% for most but over 90% for soy and legumes)
- Plant cell walls and some anti-nutritional factors in plant proteins account for their lower digestibility
- Slightly processed plant proteins like tofu, are highly digestible

(Geissler and Powers 2005; Messina et al 2004; Rolfes et al 2006)
Protein Quality:

Amino acid composition:

- To make proteins, a cell must have all the required amino acids available simultaneously; if one essential amino acid is missing, a cell must dismantle its own protein to obtain it.

- If an essential amino acid is supplied in less than the amount needed to support synthesis it is called a limiting amino acid.

(Geissler and Powers 2005; Messina et al 2004; Rolfes et al 2006)
Protein Quality:

**High quality proteins:** contain all the essential amino acids in relatively the same amounts as humans require; all foods of animal origin belong to this group.

**Low Quality / complementary proteins:** some essential amino acids are present in lower amounts - most plant foods belong to this group.

(Geissler and Powers 2005; Messina et al 2004; Rolfes et al 2006)
Focus: Misunderstanding About Protein Quality

• Vegetarian protein: it was suggested that if a protein was low in certain AAs it needed to be complemented with another protein in the same meal that contained the AA at higher levels: e.g. rice (low lysine) with beans (lower in methionine)

• Today: this concept has been declared as incorrect over the last 20 years, and new updated information is available in the newest textbooks of human nutrition – see Lecture Guides.

Comment - Dr. D. Joe Millward, The Centre for Nutrition and Food Safety, Univ of Surrey - ‘Contrary to general opinion, the distinction between dietary protein sources in terms of the nutritional superiority of animal over plant proteins is much more difficult to demonstrate and less relevant in human nutrition.’ (Millward 1999a)
Protein Requirements/Bioavailability

<table>
<thead>
<tr>
<th>Food</th>
<th>Amino Acid Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmon</td>
<td>79</td>
</tr>
<tr>
<td>Polished Rice</td>
<td>89</td>
</tr>
<tr>
<td>Whole Wheat</td>
<td>64</td>
</tr>
<tr>
<td>Potato</td>
<td>67</td>
</tr>
<tr>
<td><strong>Egg</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Protein is indispensable to life

• Protein deficiency can have devastating effects

• Protein excess, however, can be harmful too
<table>
<thead>
<tr>
<th>Situation</th>
<th>Protein</th>
<th>Protein (%) of calories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal requirements</td>
<td>20-30 grams</td>
<td>4%-5%</td>
</tr>
<tr>
<td>Recommended levels</td>
<td>45-60g</td>
<td>7%-15%</td>
</tr>
<tr>
<td>Traditional Asian Diet</td>
<td>40-70 grams</td>
<td>8%-14%</td>
</tr>
<tr>
<td>Western Diet</td>
<td>75-160 grams</td>
<td>15%-32%</td>
</tr>
<tr>
<td>Zone Diet</td>
<td>150 grams</td>
<td>30%</td>
</tr>
<tr>
<td>Atkins Diet</td>
<td>150-350 grams</td>
<td>30%-70%</td>
</tr>
</tbody>
</table>

(Rolfes et al 2006; Messina et al 2004)
Protein Calculator for your clients:

- Look up the healthy weight for a person of your client’s height
- If your client’s weight falls within that range, use it for the following calculations
- If your client’s weight falls outside the range, use the midpoint of the healthy weight range as your reference weight
- Multiply kg by 0.83 to get your RDA - use appropriate values for children, pregnant and lactating women, multiply by 1 for vegans

Example - your client weighs 59 kg
- 59 x 0.83 = 49g protein
Protein Intakes/Deficiency/Excess

Health Effects of Excess Protein - according to the Joint FAO/WHO/UNU Expert Consultation on Protein and AA Requirements in Human Nutrition 2002, an intake of twice the recommended intake is likely to be safe as long as adequate alkali rich fruit and veg to buffer the protein derived acid load is consumed.

Heart Disease

• Foods rich in animal protein tend to also be rich in saturated fat
• Plant proteins tend to lower cholesterol independently of the food fat content whereas animal proteins tend to raise cholesterol
(Rolfes et al 2006; Tonstad et al 2002)

Cancer

• Animal protein has been shown to have an independent effect on some types of cancer (colon, breast, kidneys, prostate)
(Rolfes et al 2006; WCRF 1997)
Health Effects of Excess Protein

Adult Bone Loss (Osteoporosis)

• When protein intake is high, calcium excretion rises

• Bones need both calcium and protein; ideal ratio of calcium: protein has not been established, but it is estimated to be 20:1

• Western diets provide average 9:1 ratio (i.e. too much protein, and relatively insufficient calcium)

• Too little protein may also compromise bone health

(Rolfes et al 2006)
Protein Intakes/Deficiency/Excess

Health Effects of Excess Protein

Weight control

• Protein-rich foods are often fat-rich foods, and may encourage weight gain
• High-protein diets are FAD diets; they cannot be maintained in the long term and are not conducive to health
• However protein is the most satiating macronutrient and has been proven quite useful in weight control programs
  (Rolfes et al 2006)

Kidney Disease

• A high-protein intake increases the work of the kidneys (deamination – ammonia - urea)
• Restricting dietary protein may help slow the progression of kidney disease and limit the formation of kidney stones in people who have those conditions
  (Rolfes et al 2006)
Health Effects of Inadequate Protein Intake

Deprivation of energy (and automatically protein) affects mostly children (500 million children in the world)

**Acute, Kwashiorkor** (recent food deprivation) - children who are thin for their height

**Chronic, Marasmus** (long-term food deprivation) - children who are short for their age

(Rolfes et al 2006)
Protein Intakes/Deficiency/Excess

Kwashiorkor

Marasmus
Protein deficiency in developed world:

**Children** whose diets are high in sugar and soft drinks and low in high quality wholefoods

**Teenagers** dieting, or consuming only highly refined/processed foods, junk food, soft drinks, sweets etc.

**Older people** whose immobility, dentition, general digestive health, living situation etc. reduces their calorific intake

**Anorexia nervosa** sufferers
Protein deficiency in developed world:

**Recovering patients** - post surgery or with infections (protein needs increase after surgery for repair; infections deplete body proteins)

**Homeless people** - those living in substandard conditions in inner cities and rural areas, people who are addicted to drugs and alcohol or with mental health problems

(Rolfes et al 2006)
In addition to protein synthesis, individual amino acids also:

• contribute to the synthesis of **hormones & neurotransmitters***

• **detoxify** thousands of chemicals

• supply **antioxidant protection**

• build **bile acids** for digestion

(Lord and Bralley 2008)
## Amino Acids – Introduction

### Common Conditions Suggesting Amino Acid Assessment:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aging</td>
<td>Decreased stomach acid output</td>
</tr>
<tr>
<td>Cancer</td>
<td>Cachexia</td>
</tr>
<tr>
<td>Chronic fatigue</td>
<td>Mitochondrial inefficiency</td>
</tr>
<tr>
<td>Depression</td>
<td>Impaired neurotransmitter synthesis</td>
</tr>
<tr>
<td>Dietary restrictions</td>
<td>Poor protein intake</td>
</tr>
<tr>
<td>Medications to block acid release</td>
<td>Insufficient stomach acid</td>
</tr>
</tbody>
</table>

(Lord and Bralley 2008)
Glutamine Physiological Roles

- Glutamine is the most abundant AA in whole blood
- Preferred fuel for enterocytes, lymphocytes and macrophages
- Combined with alanine for nitrogen transport in the blood
- Regulation of acid/base balance as precursor for urinary ammonia
- Substrate for citrulline and arginine synthesis in the gut
- Precursor of nucleic acids, amino sugars, proteins
- Conditionally essential – stress states; injury, sepsis, inflammation
- Glutamine is a precursor to the synthesis of glutamate
- Glutamine is involved in a glutamine-glutamate-GABA neurotransmitter function in the brain

(Lanham-New, MacDonald and Roche 2001; Liska et al 2004; Lord and Bralley 2008; Plaskett 2004)
Amino Acids in Human Health

Glutamine - Intestinal Repair & Protection

- Studies suggest that glutamine stimulates intestinal mucosal growth and protects from mucosal atrophy
- Glutamine also prevents intestinal mucosal damage and decreases bacterial component leakage across the intestinal wall
- Mechanism of action = strengthening epithelial tight junctions

(Daniele et al 2001; Klimberg et al 1990)
Glutamine - Immune Support

- It appears that glutamine has an immune-modulating effect
- High levels of cortisol in the body appear to deplete glutamine stores
- The ability of lymphocytes to proliferate and generate killer cell activity has been found to be glutamine dependent

(Hiscock et al 2003; Piccirillo et al 2003; Noyer et al 1998)
Amino Acids in Human Health

Glutamine - Clinical Applications

**Intestinal permeability**, often accompanying:

- inflammatory bowel disease
- irritable bowel syndrome
- coeliac disease
- alcohol overuse
- adult and child asthma
- NSAID-treated patients (e.g. in arthritis)

Amino Acids in Human Health

Glutamine - Clinical Applications

Chemotherapy and radiation side effects:
• Chemotherapy and radiation can injure rapidly dividing intestinal cells
• Some studies* show have shown that during chemotherapy and radiotherapy, glutamine can reduce degeneration of intestinal mucosa, prevent intestinal mucosal injury, protect liver function through enhanced glutathione biosynthesis, increase immune function, and reduce permeability of the gut (although limited results in more intense chemotherapies)

*Note - Not all studies have shown that glutamine is safe to use during chemotherapy

(Wu et al 2004; Piccirillo et al 2003; Yu et al 1999)
Glutamine - Clinical Applications

Peptic ulcers:

- **Cabbage juice**, a key source of glutamine, is well documented as successful in treating peptic ulcers

- One litre per day of the fresh juice, taken in divided doses, resulted in total ulcer healing in an average of only ten days

- Further research has shown that the high glutamine content of the juice is probably responsible for the efficacy of cabbage in treating these ulcers

(Harward et al 1994)
Glutamine -Clinical Applications

Human Immunodeficiency Virus:
• Loss of body mass and drug-associated gastrointestinal problems often occur in patients with HIV infection
• Given the role glutamine plays in reversal of malabsorption, and protection of the small intestine, glutamine deficiency is a probable factor in HIV-associated wasting
• Some studies suggest improvements in HIV-positive patients dosed at 8 g a day with regard to intestinal permeability and intestinal absorption

(Klimberg 1990; Shabert et al 1996; Noyer et al 1998; )
Amino Acids in Human Health

Glutamine Supplementation

- Delivery method and effective dosage should be condition specific

- Glutamine breaks down quite rapidly in solution – powdered products should be consumed as soon as possible after being mixed with liquid

- Osieki recommends between 500 – 3000mg per day, up to 30g/day in trauma cases.

- Lysine amplifies GABA action on the brain

(Liska et al 2004; Osieki 2010)
Amino Acids in Human Health

Glutamine Supplementation

- **Peptic ulcers**: drinking one litre a day of cabbage juice in divided doses or 1.6 g/day of glutamine for one month

- **HIV patients**: 30 to 40 g glutamine/day to prevent medication-associated diarrhoea, and to improve intestinal permeability; co-administration of antioxidants may also be helpful

(May et al 2002; Huffman et al 2003; Shabert et al 1999)
Glutamine Intake/Supplementation - Toxicity

Effects of excessive glutamine supplementation:

• Review of chronic effects of glutamine concludes that no adverse effects are reported during short-term dosing up to 50-60g/day

• However patients under long-term supplementation should be monitored for metabolic diseases like diabetes, coronary artery disease and psychological changes due to glutamate’s neurotoxic effects*

(Garlick 2001)
Glutamine Intake/Supplementation – Drug Interactions

• Many anti-seizure medications including **phenobarbital, phenytoin, carbamazepine, primidone and valproic acid** work to block glutamate activity in the brain

• Because glutamine can convert to glutamate, supplementation in patients using these medications should be done with caution (always check with the GP!)

(Murray and Pizzorno 2008)
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Glutamate/ Glutamic Acid

• Neurotransmitter – principal excitatory amino acid in the brain, involved in movement, cognition memory and sensation

• Precursor for GABA synthesis

• Agonist for umami taste receptor

• Substrate for glutathione synthesis

(Lanham-New, MacDonald and Roche 2001; Liska et al 2004)
Glutamate - Genesis of Glutathione

- **Glutathione** is a tripeptide consisting of *glutamate, cysteine, and glycine* - an important antioxidant

- Glutathione has a sulphur element (because of cysteine) – detoxifies and neutralises substances such as chlorine

(Yu et al 1999; Flaring 2003, Cao et al 1999)
Glutamate/Glutamic Acid Supplementation - Toxicity

Effects of glutamic acid supplementation:

Glutamic acid is not generally used in clinical interventions because of neurotoxic effects from administration of the free amino acid.

Reports of those effects have generated public controversy over regulation of MSG as a food additive.

(Lowe 1990; Lord and Bralley 2008)
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Glutamate/Glutamic Acid Intake & Supplementation - Toxicity

Chinese Restaurant Syndrome


Free access (google scholar)
Arginine/Ornithine/Citrulline Physiological Roles

• Three main amino acids essential for the functioning of the Urea Cycle - a cycle of biochemical reactions producing urea (NH$_2$)$_2$CO from ammonia (NH$_3$)

• Urea Cycle is a way of disposing of a very toxic compound (ammonia) by converting it to a less toxic one

(Lord and Bralley 2008)
Arginine/Ornithine/Citrulline - The Urea Cycle:

KEY TO ENZYMES (Circled Numbers)
1. Carbamoyl-phosphate synthase (ammonia)
2. Ornithine carbamoyltransferase
3. Argininosuccinate synthase
4. Argininosuccinate lyase
5. Arginase
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Arginine/Ornithine/Citrulline - The Urea Cycle

Impairments of the liver’s Urea Cycle can lead to **Hyperammonaemia**:

- Chronic fatigue
- Headache
- Irritability
- Nausea and diarrhoea
- Lack of concentration
- Mental confusion
- Intolerance of high protein foods

(Lord and Bralley 2008)
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Arginine - Clinical Applications:

• Arginine is the precursor of nitric oxide (involved in endothelial relaxation*, neurotransmission, thyroid activity regulator)
• Reading: revise the functions of NO

Arginine → Citrulline + nitric oxide (NO)

• Nitric oxide synthesis is blocked by high fat meals, high blood homocysteine levels, low antioxidant status, lack of exercise.

(Lord and Bralley 2008; Tousoulis et al 1998; Boger et al 1998; Fard et al 2000)
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Arginine - Clinical Applications

• There is evidence of arginine deficiency in coronary artery disease - arginine administration in angina patients with narrowed coronary arteries resulted in greater dilation of diseased arteries

• May accelerate wound healing – collagen synthesis

• Is needed for sexual maturity and is necessary for normal sperm count and motility; improves erectile function, although responses can vary

(Tousoulis et al 1998; Perez-Amador et al 2002; Aydin et al 1995)
Arginine - Supplementation

• The only proven clinical application of supplemental arginine = **heart disease**
  (improvement of the endothelial function, improvement of vasodilation)

• **Dosage 5.6 to 12.6 g/day**

• **Caution:** arginine competes with lysine and histidine for intestinal transport; long-term supplementation should be done with caution

( Rector et al 1996 ; Hambrecht 2000)
Arginine - **Toxicity**

Oral supplementation of L-arginine can cause:

- abdominal pain, bloating, diarrhoea
- gout
- exacerbation of airway inflammation in asthma
- exacerbation of herpes infections

(Brittenden 1999; Rector et al 1996; Takano et al 1998)
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Arginine - Drug Interactions

Caution - Arginine can interact with:

- antihypertensive drugs
- nitrates
- sildenafil (viagra)

(Cheng and Balwin 2001)
**Branched Chain Amino Acids (BCAA): Valine, Leucine, Isoleucine - Physiological Roles**

- BCAAs make up 35% of muscle proteins and 50% of AA in dietary proteins
- Directly stimulate protein synthesis, fully oxidised in mitochondria for energy, within the liver can act as precursors for lipids or ketone bodies

(Lika et al 2004; Lord & Bralley 2008)

**Clinical Applications**

- BCAAs inhibit muscle proteolysis which can have a positive muscle sparing effect during exercise
- Oral administration appears to inhibit muscle glycogen degradation during exercise
- BCAA supplementation also attenuates N loss and protein wasting during bed rest

Branched Chain Amino Acids (BCAA): Valine, Leucine, Isoleucine - Clinical Applications:

Anorexia:

• Diets deficient in BCAA might be associated with decreased appetite and anorexia

• Mechanism - BCAA compete with tryptophan (a precursor for serotonin) phenylalanine and tyrosine for uptake across the blood brain barrier as they share a transport mechanism. Research suggests high levels of serotonin are responsible for cancer anorexia. By decreasing the synthesis of serotonin - BCAA might increase appetite.

(Gietzen and Magrum 2001; Hiroshige et al 2001; Liska et al 2004)
Branched Chain Amino Acids (BCAA): Valine, Leucine, Isoleucine

Diet
- Particularly concentrated in the germs of grains, in fish and dairy products
- Deficient levels in grain flours and most nuts/seeds

Supplementation
- Supplementation of malnourished elderly patients with BCAA seems to improve appetite and improve nutritional status
DOSE 12 g daily in capsules

Branched Chain Amino Acids (BCAA): Valine, Leucine, Isoleucine - Drug Interactions

BCAA can interact with:

• anti-diabetes medication

• levodopa (anti-Parkinson’s medication)

• corticosteroids

(Hutson et al 2001; Harris et al 2001; DiPiro et al 1999)
Branched Chain Amino Acids (BCAA): Valine, Leucine, Isoleucine - Toxicity

- Liver function should be monitored if high doses or long-term use of branched chain amino acids is used.

- Short-term use of 60 g of BCAA for seven days in patients with normal metabolic function seems to increase levels of ammonia, but not to toxic plasma levels.

(Scarna et al 2003)
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Methionine, Cysteine - Sulphur Amino Acids - Physiological Roles

- **Methionine** can be converted into SAM (s-adenosylmethionine) a major methyl (-CH$_3$) donor in the body and is required for the *synthesis of acetylcholine, creatine, and epinephrine*

- **Cysteine** is synthesised from methionine; is a *component of glutathione, co-enzyme A and taurine*

(Lord and Bralley 2008)
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Methionine – Clinical Applications:

• **Hyperhomocysteinaemia** might increase the risk for vascular disease

• Hyperhomocysteinaemia that is unresponsive to vitamin supplementation sometimes responds to dietary restriction of methionine

• Methionine rich foods include: eggs, fish, turkey, cheese and chicken

(Ward et al 2000; Bellamy 1998; Barshop 2000; Osieki 2010)
Methionine – Clinical Applications:

- Methionine might act synergistically with folate to decrease the risk of colon cancer.
- However, there is also evidence a high dietary intake of methionine with salt and nitrates might increase the risk of gastric cancer.

  **Note** - Rates of methylation are much higher in tumour tissue than in normal tissue and most tumours are dependent on exogenous, preformed methionine for growth.

- Preliminary clinical evidence suggests restriction of dietary methionine in cancer patients might inhibit tumour growth and improve cancer treatment outcomes.

(Su and Arab 2001; LaVecchia et al 1997; Epner 2001; Epner et al 2002)
Methionine Toxicity

- **Atherosclerosis**: dietary or supplemental methionine can increase homocysteine levels especially in patients who are deficient in folate, vitamin B12, or B6, or patients who have disorders of homocysteine metabolism.

- Hyperhomocysteinaemia is associated with an increased risk for vascular disease.

(Anon 1997; Bellamy et al 1998a; Hladovec et al 1997; Ward et al 2000)
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Methionine Toxicity

- **Cancer**: most tumours are dependent on exogenous, preformed methionine for growth. There is some evidence that restriction of dietary methionine in cancer patients might inhibit tumour growth and improve cancer treatment outcomes.

- **Liver disease and cirrhosis**: methionine may aggravate existing liver damage in patients with liver disease.

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Cysteine - Physiological Role

- Most sulphur in food is in the form of protein-bound cysteine.
- High-sulphur foods include eggs and legumes (high cysteine foods).
- Cysteine is the source of sulphate (-SO₄), used in the phase II liver detoxification pathway - sulphation (used for many drugs, steroid hormones etc.).
- Sulphation increases water solubility of many hydrophobic compounds in preparation for their excretion in urine.

(Lord and Bralley 2008)
Cysteine - Physiological Roles

• **N-acetyl cysteine (NAC)** is a derivative of the amino acid L-cysteine used in supplementation (for functions of NAC see next slide)

• Cysteine is made from methionine and serine in liver (vitamin B6, B12 & folate are needed)

• Cysteine is a **precursor of glutathione**, which is a potent antioxidant

(Weinbroom et al 2000; Kelly 1998)
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Cysteine Physiological Roles

• The antioxidant effects of N-acetyl cysteine may explain its ability to prevent adverse effects caused by toxic chemicals and drug reactions (e.g. acetaminophen overdose)

• The antioxidant and free radical properties might also make N-acetyl cysteine useful in the treatment of pulmonary and cardiac disease

• N-acetyl cysteine also appears to reduce cellular production of proinflammatory mediators

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Cysteine - Physiological Roles

• N-acetyl cysteine can impair platelet aggregation

• In patients with HIV, N-acetyl cysteine can increase levels of glutathione

• Increased concentration of glutathione seems to reduce oxidative stress associated with HIV disease and to improve the number and activity of CD4 T-lymphocytes

(Anfossi et al 2001; De Rosa et al 2000)
Cysteine - Supplementation:
Cysteine supplementation (relevant in nutrition therapy) seems to be effective in:

- bronchitis (to reduce exacerbations of chronic bronchitis) 200-600 mg twice a day
- influenza (reducing symptoms) 600 mg twice a day
- hyperhomocysteinaemia 1.2 g once a day
- chronic obstructive pulmonary disease (COPD). Supplementation can decrease the number of acute exacerbations by about 40% when used in addition to standard therapy - 600 mg once a day

(Grandjean et al 2000; Wiklund et al 1996; Pela et al 1999)
Cysteine - Toxicity

- Orally, N-acetyl cysteine can cause gastrointestinal adverse effects including nausea, abdominal pain, vomiting, constipation, and diarrhoea, particularly when used in high doses.

(De Rosa et al 2000; Oldemeyer et al 2003; Ellenhorn 1997)
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Cysteine - Drug Interactions

- **Nitroglycerine**: concomitant administration of N-acetyl cysteine and intravenous nitroglycerin can cause severe hypotension and intolerable headaches

- May interfere with insulin function in diabetics

(Horowitz et al 1988; Ardissino et al 1997)
Carnitine - Physiological Functions

• Carnitine is an amino acid derivative synthesised from methionine and lysine (cofactors: Fe, vit C and vit B3, B6 – lack of cofactors reduces biosynthesis)

• The body obtains some carnitine from the diet; primarily from red meats and dairy products, nuts, seeds, some vegetables

• Carnitine aids in cellular energy production by transporting LC fatty acids into mitochondria for oxidation. Mobilises fatty acids, (reduces surface fats- cellulite) takes fats into cells where they are used for energy – reduces levels of triglycerides in blood and reduces cholesterol

• Deficiency of carnitine (rare) results primarily from errors of metabolism, and not from insufficient dietary intake, as the body is usually able to synthesise adequate quantities

• Genetic or medical issues can make it a conditionally essential AA

(Lenzi et al 2004; Gropper et al 2005)
Amino Acids in Human Health

Carnitine - Clinical Applications:

Carnitine deficiency presents with:

- symptoms of progressive cardiomyopathy
- skeletal muscle weakness
- fasting hypoglycaemic coma

(Stanley 2004)
Carnitine - Clinical Applications
Carnitine therapy has been shown to be effective in:

- congestive heart failure (symptom improvement)
- infertility (improved sperm morphology & motility)

(Rizos 2001; Benvenga et al 2001; Lenzai et al 2004)
Carnitine - Clinical Applications

There is as yet insufficient evidence to promote carnitine supplementation in:

- athletic performance
- ADHD
- Fatigue - related to age, cancer, MS, HIV or Coeliac disease. However research is ongoing – read [http://www.jspsmjournal.com/article/S0885-3924(06)00554-9/abstract](http://www.jspsmjournal.com/article/S0885-3924(06)00554-9/abstract) and [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4340370/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4340370/)
Carnitine - Supplementation

• Congestive heart failure (symptom improvement)
  1 g twice daily

• Hyperthyroidism (symptom improvement)
  1-2 g twice daily

• Infertility (improvement of sperm count & motility)
  2 g of L-Carnitine plus 1 g L-acetyl-carnitine daily

• Carnitine is used medically for Hepatic Encephalopathy

(Rizos 2001; Benvenga et al 2001; Lenzai et al 2004)
Carnitine - Toxicity

- L-carnitine used orally or intravenously has been associated with nausea, vomiting, abdominal cramps, heartburn, gastritis, diarrhoea, body odour and seizures

- One of its metabolites can cause the urine, breath and sweat to have a fishy odour

(Evans and Fornasini 2003)
Carnitine - Drug Interactions

**Acenocoumarol** (anticoagulant) - 1 g/day seems to significantly increase the anticoagulant effects of acenocoumarol

**Thyroid-hormone** - L-carnitine appears to act as a peripheral thyroid hormone antagonist by inhibiting entry of thyroid hormone into the nucleus of cells. Theoretically, taking L-carnitine might decrease the effectiveness of thyroid hormone replacement

**Warfarin** (anticoagulant) - although no data available, carnitine may increase the anticoagulant effects of warfarin similarly to its interaction with acenocoumarol

(Bachmann et al 2004; Benvenega et al 2004)
Creatine Physiological Roles

- Small peptide made of amino acids, arginine, glycine and methionine
- Source of fast energy for muscles via creatine phosphate
- Can be obtained from foods (mainly meat, fish) and it is synthesised in the body (liver, kidney, pancreas)
- About 95% of body creatine is in muscle; 5% in other organs
Creatine - Clinical Applications

• Evidence suggests that creatine supplementation may help athletes enhance muscle performance during repeated bouts of brief, high-intensity exercise

• However, for other exercise creatine appears to offer no benefit

(Kreider et al 1998; Leenders et al 1999; Rossouw 2000; Cooke et al 1997; Van Schuylendergh et al 2003)
Creatine - Clinical Applications

- In patients with congestive heart failure (CHF), cardiac ATP is lower than in people with normal cardiac function and correlates with the severity of heart failure.

- Creatine phosphate appears to improve congestive heart failure by preventing oxidative damage, and improving microcirculation.

- In the case of CHF oral creatinine supplementation was not effective - intravenous supplementation was used.

(Kreider et al 1998; Leenders et al 1999; Rossouw 2000; Cooke et al 1997; Van Schuylenbergh et al 2003)
Creatine - Clinical Applications

• Some evidence also suggests that creatine might be useful in Parkinson's disease, possibly due to neuroprotective effects

• Taking creatine can decrease the rate of disease progression compared to placebo in early Parkinson's disease patients who do not need medications for symptom control

(Matthews et al; NINDS 2006)
Creatine - Supplementation

- Skeletal muscle has a saturation point beyond which additional supplemental creatine will not increase intracellular creatine levels. This point occurs within the first few days of loading.

- Exogenous creatine supplementation also appears to reduce endogenous creatine production.

- After discontinuing supplementation, endogenous creatine production and creatine levels typically return to baseline within 28 days.

(Persky et al 2003; Terjung et al 2000)
Amino Acids in Human Health

Creatine - Supplementation

• **Athletic performance**: various dosages have been used, most commonly -0.3g/kg body weight for five days (acute loading) followed by maintenance (0.03g/kg body weight)

• **Parkinson’s disease**: various regimes have been used; most commonly 10g/day

(Juhn 1999; NINDS 2006)
Amino Acids in Human Health

Creatine - Drug Interactions

• Combining caffeine, ephedra and creatine may lead to ischaemic stroke

• High doses of creatine might adversely affect renal function & combining creatine with potentially nephrotoxic drugs might have other harmful effects on kidney function

**Nephrotoxic drugs**: cyclosporine; aminoglycosides including amikacin, gentamicin and tobramycin, nonsteroidal anti-inflammatory drugs (NSAIDs) including ibuprofen, indomethacin, naproxen and numerous others

(Vahedi et al 2000; Terjung et al 2000)
Glycine - Physiological Roles

• **Conditionally essential** amino acid in the case of certain metabolic stresses (increased haem synthesis for blood formation, collagen formation for growth and repair, glycine conjugation in detoxification, etc.)

• Glycine is required for the *synthesis* of haem pigment in RBCs, DNA, RNA, bile acids, glutathione (liver detox), skin & connective tissue

• Collagen, the most abundant protein in the body is 1/3 glycine

• All enzymes, transport proteins, and membrane receptors contain approximately 10% glycine

(Lord and Bralley 2008)
Glycine - Physiological Roles

• Detoxification - glycine binds to a toxic substance forming a less toxic substance that can be excreted from the body - amino acid conjugation

• Neurotransmitter -
  – glycine is reversibly converted to serine
  – serine is a critical component in the biosynthesis of acetylcholine
  – depressed patients have lower glycine levels than controls

(Lord and Bralley 2008; Altamura et al 1995)
Amino Acids in Human Health

Taurine Physiological Roles

- It has a sulfonic acid group rather than a carboxyl group so is not strictly an amino acid
- Antioxidant roles in various tissues
- Assists fat metabolism
- Helps fat digestion by maintaining bile salt solubility
- Enhanced insulin production

(Lord and Bralley 2008)
Taurine - Physiological Roles

Food sources: meat, fish & breast milk

Taurine is important for:

- the development of the cerebellum and retina
- bile acid conjugation – end products of taurine conjugation are very soluble therefore flow better from the liver
- taurine should be considered essential for neonates and should be included in total parenteral nutrition solutions for these and any other patient requiring parenteral nutrition to avoid metabolic cholestasis (a condition where bile cannot flow from the liver to the duodenum)
- white blood cell antioxidant activity
- CNS neuromodulation
- platelet aggregation, sperm motility, insulin activity.

(Lord and Bralley 2008; Anon 1975, Howard and Thompson1992, Lourenco and Camilo 2002)
Amino Acids in Human Health

Taurine Supplementation

• Taurine is normally synthesised in the human body in adequate amounts from cysteine
• During prolonged times of insufficient intake, such as during parenteral nutrition, the body cannot maintain adequate levels of taurine and supplementation becomes necessary
• Supplementation is also necessary in non-breastfed infants because their ability to synthesise taurine is undeveloped and cow's milk does not provide a sufficient amount
• Therefore taurine is often added to human infant formulas, enteral products, and some parenteral nutritional solutions
• Excess taurine is excreted by the kidneys

(Niittynen et al 1999)
Theanine - Physiological Roles

- The amino acid found uniquely in green tea, non-essential considered non-dietary AA
- Oral ingestion crosses the BBB. Standard dose 50-250mg. Effects noted approx. 40 minutes after ingestion
- Blocks the binding of glutamic acid to glutamate receptors
- Helps increase alpha brain waves producing a calming, mood-enhancing effect without drowsiness. Reduces perceived stress in human subjects

(Nobre, Rao and Owen 2007; Kimura et al 2007)
Amino Acids in Human Health

Theanine - Clinical Applications

- Improving learning performance, heightening mental acuity, and promoting concentration
- Calming nervous agitation
- Lowering blood pressure
- Diminishing symptoms of PMS
- Studies indicate that theanine produces these effects by increasing the level of GABA, an important inhibitory (sedative) neurotransmitter in the brain. Theanine also appears to increase levels of dopamine, another brain chemical with mood-enhancing effects, which can reduce blood pressure

(Yokogoshi et al, 1995)
Theanine – Supplementation

- It is estimated that the quantity of green tea consumed by the average Japanese tea drinker per day contains about 20 mg of theanine but there are no studies measuring the amount of theanine being extracted by typical preparation methods.

- The therapeutic range for theanine in human trials has been between 50mg-200mg.

(Kimhura et al 2007; Yokogoshi et al 1998)
Amino Acids in Human Health

Tyrosine - Physiological Roles

• Derived from phenylalanine and a precursor of the thyroid hormones, dopamine, epinephrine (adrenaline), norepinephrine (noradrenaline) and melanin

• Increases alertness, regulates blood pressure, stimulates prolactin secretion

Tyrosine - Clinical Applications

• Adrenal and/or mental exhaustion
• Depression
• Anxiety & PMT
• Appetite control
• Hypo & hypertension

(Osiecki, 2010)
Amino Acids in Human Health

Tyrosine – Supplementation

- Supplemental range: 400-6000 mg

- **Caution**: if dosage exceeds 3% of the diet corneal lesions, eye problems, palm and sole erosions and skin lesions may result

- **Contraindicated** with the antidepressants MAOIs - monoamine oxidase inhibitors

- **Contraindicated** – melanoma (skin cancer) or glioblastoma (brain tumour)

(Osiecki 2010)
Tryptophan: Essential AA. Dietary sources: brown rice, dairy, chicken, fish, nuts, soy

Physiological Functions
• Production of niacin (B3)
• Production of serotonin which plays a role in combating depression and insomnia and helps to stabilise mood

Clinical Applications:
• Helps to control hyperactivity in children, alleviates stress and anxiety, fibromyalgia, aids weight control by reducing appetite, and enhances the release of growth hormone thus making it an item of interest for anti-ageing studies

Supplemental range: 100 to 600 mg/day

Note: Tryptophan was banned as a supplement for approximately 20 years due to 38 deaths, believed now to be as a result of supplement contamination

(Balch 2006, Osiecki 2010)
**Phenylalanine**: Essential AA. Dietary sources: almonds, avocado, brown rice, cheese, eggs, fish, lentils, meat, soy

**Physiological Functions:**
- Phenylalanine can cross the blood brain and therefore has a direct effect on brain chemistry
- Phenylalanine can be converted to tyrosine which in turn used to synthesise dopamine, epinephrine, norepinephrine, melanin and thyroid hormones
- Because of this relationship this AA is believed to elevate mood, decrease pain, aid in memory and learning, and suppress the appetite

(Balch 2006, Osiecki 2010)
Phenylalanine:

Clinical Applications:
• Agitation, appetite control, memory loss, kidney failure
• Various types of chronic pain – studies show mixed results
• Depression - some clinical studies suggest that phenylalanine may be helpful as part of a comprehensive therapy for depression. However, most of the studies were done in the 1970s and 1980s and were not rigorously tested
• Parkinson's disease – animal studies have shown improvement in rigidity, walking disabilities, speech difficulties, and depression associated with Parkinson's disease – needs further research

Contraindicated in those with phenylketonuria, pregnant or lactating women and those on antipsychotic or neuroleptic medications

Note: can cause anxiety, headaches and hyperactivity in children

Supplemental Range: 150 to 1200 mg/day

(Balch 2006, Osiecki 2010)
Lysine: Essential AA. Dietary sources: chicken, egg, dairy, fish, red meats, soy products

Physiological functions:
• Promotes growth and bone development in children
• Evidence suggests lysine assists iron and zinc absorption
• Moderates triglyceride levels
• Required for antibodies, hormone and enzyme formation
• Helps with collagen formation and tissue repair
• Increases intestinal absorption of calcium

(Balch 2006; Rushton 2002, Osiecki 2010)
Amino Acids in Human Health

Lysine: Clinical Application

- Helps to build muscle - therefore useful for those recovering from surgery and sports injury
- May also be useful in athletic performance
- Osteoporosis
- Alleviates postherpetic nerve pain
- Hyperglycaemia
- Herpes/cold sores – supplemental L-lysine plus vitamin C with bioflavonoids helps to fight or prevent herpes outbreaks
- Research suggests L-lysine helps combat hair loss, particularly in women (could be due to improved iron absorption/transport)

Supplementation range: 300-3000 mg/day

Note: Lysine is the limiting amino acid in most cereal grains; also it competes with arginine for absorption; levels in excess of 10-15 g per day can cause nausea, vomiting, diarrhoea

(Balch 2006; Rushton 2002, Osiecki 2010)
Amino Acid Supplementation Guidelines

General Guidelines

• Amino acids **compete with each other** at the cell surface for transportation through the membrane

• Using just one amino acid (or a small number of a.a.) gives that amino acid an advantage in terms of absorption

• This may serve therapeutic purpose in the short term, but in the **long term** it can lead to **imbalance**!

• Long-term amino acid therapy should be done with specifically selected amino acids in conjunction with a complete Free-Form Amino Acid Formula
Amino Acid Supplementation Guidelines

Amino Acid Supplementation Naturopathic Rationale

• Many cell functions can be restored by providing amino acids to assist neurotransmitter and hormone synthesis

• The physical and immunologic barriers in the gut can be restored

• Blood glucose can be stabilised through better gluconeogenesis

(Plaskett 2004)
Amino Acid Supplementation Naturopathic Rationale

• Utilisation of fatty acids for energy is enhanced by better mitochondrial performance

• Hepatic and gastrointestinal detoxification reactions are improved when AAs required for conjugation reactions are available

• Oxidative damage is reduced when sulphur amino acid supply is adequate to maintain glutathione

(Plaskett 2004)
Amino Acid Supplementation Naturopathic Rationale

**Goal** - to break the vicious circle where patients/clients - sometimes despite excess protein intakes - cannot utilise protein properly which results in -

- limited protein synthesis
- limited detoxification capacity
- impaired hormone/neurotransmitter synthesis

(Plaskett 2004)
Amino Acid Supplementation Guidelines

Free-Form Amino Acid Supplement Formulas

• The ratios of amino acids in a free-form amino acid base formula are set according to optimal human needs
• The cofactors like vitamin $B_6$ are added to ensure interconversions leading to nonessential amino acids
• These supplements have little flavour though in most cases mixing with fruit juices or food is sufficient to improve palatability
• Because of their free (non-peptide linked) form, the amino acids are very efficiently absorbed, even in the absence of stomach acid and pancreatic secretions

(Lord and Bralley 2008)
Amino Acid Supplementation Guidelines

Amino Acid Supplementation - Cofactors

• Major reason for impaired utilisation of amino acids is dietary lack of micronutrients used in amino acid interconversions like Zn, vit B₆, vit B₁₂

• Always try to address the diet first

(Lord and Bralley 2008)
Amino Acid Supplementation - **Toxicity**

**Effects of excessive protein/AA intakes are seen as:**
- increased urea excretion
- increased LDL levels (animal protein only)
- calcium loss
- calcium oxalate stone formation
- progression of renal disease

THANK YOU