Lipids and Essential Fatty Acids

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Learning Outcomes:
On successful completion you will be able to:

• Describe the structural characteristics of lipids and fatty acids
• Outline the dietary sources, function, bioavailability and metabolism of fatty acids, including EFAs
• Discuss the deficiency states, therapeutic uses and safety considerations that apply to EFAs
Lipids

• Lipids are not a coherent group of compounds, like the carbohydrates or proteins.
• The lipids are made up of several very different types of compounds
• They are generally characterised by not mixing with water
• Liver and adipose cells can synthesise lipids from glucose or amino acids through lipogenesis which is stimulated by insulin
Function of lipids

- **Energy production**
- **Storage** Excess fat is stored for future energy production
- **Insulation** Subcutaneous adipose tissue helps to maintain normal body temperature
- **Protection** Internal (visceral) fat protects internal organs such as the kidneys and spleen
- **Absorption** Dietary fat is needed for the absorption of fat-soluble nutrients
- **Cell Membranes** Lipids are essential components of all cell membranes
- **Brain** Several types of lipids are essential for brain function
- **Hormones** Steroid hormones are important in/for stress, sex, immune function, mineral control
- **Many information and control molecules** are made of lipids or are lipid-soluble
Risks

- Processed and over heated fats can be altered to create toxic compounds.

- Accumulation of excessive visceral fat (abdominal obesity) is a risk factor for heart disease, diabetes, and is linked to insulin resistance.

(Rolfes et al 2006; Geissler and Powers 2005)
Lipids exist in the body in several forms

- Individual fatty acids
- Triglycerides
- Phospholipids
- Sphingolipids
- Glycolipids
- Cerebrosides
- Cholesterol and related steroid based compounds
- Fat-soluble vitamins
- Waxes
Fatty acids – chain length

- Fatty acids are long hydrocarbon chains with an acid group at one end
- Most fatty acids have an even number of carbon atoms
- Short and medium chain fatty acids are absorbed into the portal vein, transported to the liver and circulated attached to albumin
- Long chain fatty acids are absorbed within chylomicrons
- Short chain fatty acids have up to 5 carbon atoms
- Medium chain fatty acids have 6-12 carbon atoms
- Long chain fatty acids have up to 14-22 carbon atoms
- Very long chain fatty acids have more than 22 carbon atoms
Short chain fatty acids

- Butyric acid, (C4) found in (cow, sheep and goat) milk, cream and butter
- Released from the triglyceride when milk goes rancid and provides the smell of rancidity
- Improve calcium absorption
- Produced by anaerobic gut fermentation
- Butyrate inhibits colonic tumour cells, and promotes healthy colonic epithelial cells

Medium chain fatty acids

- Diffuse from the small intestine to the portal system
- Do not need energy for their absorption
- Do not need bile for their absorption
  - Useful in biliary insufficiency and malabsorption problems

- Examples: caprylic (C8), capric (C10), lauric (C12)
Long chain fatty acids

• Absorbed within chylomicrons, more on these later
• Examples
  – Palmitic acid
  – Oleic acid
  – Stearic acid
  – The essential fatty acids
Unsaturated fatty acids

- Unsaturated fatty acids contain one or more double bonds.
- These can be saturated by the addition of hydrogen – as in hydrogenation when oils are made into solid spreads.
- Monounsaturated fatty acids have 1 double bond in the chain.
- Poly unsaturated fatty acids have several double bonds in the chain.
- Omegsa-3 fatty acids start the first double bond 3 carbon atoms from the CH3 end.
- Omega-6 fatty acids start the first double bond 6 carbon atoms from the CH3 end, etc.
- There are usually 3 carbon atoms between each double bond.
- Thus if the double bonds are oxidised the breakdown products are the 3-carbon atom segments that turn into (potentially mutagenic) malondialdehyde.
Cis and trans fatty acids

- At each double bond two possible isomeric forms exist.
- i.e. the two chains on either side can either be on the same side of the double bond (cis) or the opposite sides (trans)
Trans fatty acids

- Biological systems, plants, animals, humans, including food oils are Cis fatty acid

- The trans fatty acids:
  - Are less effective
  - Can be harmful
  - Can interfere with the function of the cis forms
Essential fatty acids

• There are two fatty acids that cannot be made in the body and so are ‘essential in the diet’
• Linoleic acid and alpha-linolenic acid
• Arachidonic acid was once thought to be essential in the diet, but we now know it can be made from linoleic acid
Essential Fatty Acids-Introduction

• In the course of evolution, human beings lost the ability to make enzymes that catalyse the introduction of double bonds into fatty acids between the carbon atoms 6-7 and 3-4 (LA, ALA)

• These fatty acids need to be supplied with diet – i.e. they are essential= Essential Fatty Acids (EFA)

• EFA levels are determined primarily by dietary intake, though sex hormone levels, can have an effect too

(Garrow et al 2004; Jokela et al 2004; de Catalfo and de Gomez 2005)
Fatty acid melting points

- Saturated fatty acids have a higher melting point than unsaturated fatty acids.
- Hence they tend to be solid at room temperature.
- The more saturated a fatty acids the higher the melting point – e.g. mps:
  - Butter (saturated) = 32-35C
  - Coconut oil = 25C
  - Peanut oil = 3 C
  - Olive oil = -6 C
  - flaxseed oil = -24C (so store in the deep freeze)
Triglycerides structure

- Triglycerides are esters of 3 fatty acids with 3C glycerol (Esters are a combination of a carboxylic acid groups and an alcohol group)
- Thus TGs consist of 3 fatty acids and 1 molecule of the alcohol, glycerol
- The fatty acids can be the same or varied
- They can be saturated or unsaturated
- They can be short, medium, long or very long chain length
Triglycerides and energy storage

Energy Storage

- Triglycerides act as long-term fuel reserves
- Excess dietary energy from carbohydrates and protein is converted to triglycerides via lipogenesis
- The majority of unused triglycerides are stored in adipose tissue, in adipocytes (fat cells)
- Following a meal, ingested fat which is not required by tissues is also taken up by the adipose tissue
- When dietary energy is limited, the fatty acids from triglycerides are mobilised, from the adipocytes, into circulation

(Rolfes et al 2006; Geissler and Powers 2005)
Rancidity and toxicity

- Triglycerides made of saturated fatty acids go rancid by releasing the fatty acids from the glycerol e.g. the release of butyric acid from butter triglycerides.
- Triglycerides with unsaturated fatty acids can go rancid in the same way.
- They can also go rancid when the double bonds are oxidised. This generally leads to the production of malondialdehyde.
- Malondialdehyde is a potential mutagen. It is found in some hydrogenated or overheated fats.
Phosphatides

Phosphatides are based on phosphatidic acid. They contain:

- Glycerol, 2 long chain fatty acids, a phosphate group and one of the following 4: Inositol, choline, ethanolamine or serine

Thus:

- Phosphatidyl choline
- Phosphatidyl inositol
- Phosphatidyl ethanolamine
- Phosphatidyl serine

These are the main components of the lecithins
Sphingolipids and glycolipids

• Sphingolipids are phospholipids that contain the alcohol sphingosine in the molecule
• Glycolipids are phospholipids that contain a carbohydrate group in the molecule
Phospholipid functions

- Lecithin is an emulsifying agent.
- It is an essential component of bile and needed for fat digestion.
- Lecithins are essential components of the lipoproteins (discussed later).
- Phospholipids are essential components of cell membranes.
- Sphingolipids protect cell surfaces.
- Sphingolipids, glycolipids and cerebrosides have important functions in the brain.
- Some lipids are involved in cell signalling - the conversion of extracellular signals into intracellular ones.
- Inositol phospholipids are important mediators of hormone and neurotransmitter action.
Steroids

- Steroids, including cholesterol, are based on the steroid nucleus.
- The numbers refer to the position of the C atoms.
Cholesterol

Cholesterol is:

• an important and essential compound
• much and wrongly maligned

Cholesterol is essential for the synthesis or action of:

• Vitamin D and so calcium metabolism
• Cortisol, cortisone and related hormones for immune function and stress
• Aldosterone for mineral and fluid balance
• Estrogen, progesterone and other female hormones
• Testosterone and other male hormones
Cholesterol

Cholesterol is essential for the synthesis or action of (continued):

• Bile salts and acids, and so for digestion
• Brain chemistry (the brain = 2-3% of total body weight but contains 25% of the body's cholesterol
• Cell membrane integrity (‘sandwiched’ between two layers of phospholipids)
• Lipoproteins and triglyceride (TG) transport
Cholesterol synthesis and elimination

- A diet rich in TGs stimulates cholesterol synthesis
- If the diet is deficient in cholesterol more is synthesised, first in the enterocytes of the small intestines (S.I.), then in the liver
- Most cells in the body can synthesise cholesterol
- If the diet is rich in cholesterol very little additional cholesterol is synthesised
- Cholesterol is an important compound and is not catabolised within the body.
- Cholesterol is excreted in the stool intact, mostly as bile products
- This excretion is increased by absorption onto non-digestible carbohydrates
- Total cholesterol (endogenous + dietary intake) = approx 1g/daily

(Gropper et al 2005)
Cholesterol Products

Cholesterol

- Pregnenolone
  - Progesterone
    - Androgens
      - Androsterone
      - Testosterone
    - Estrogens
      - Estradiol
      - Estriol
      - Estrone
  - Mineralcorticoids
    - Aldosterone
    - Corticosterone
  - Glucocorticoids
    - Cortisol
- 7-Dehydrocholesterol
  - Cholecaliferol (vitamin D)
- 7-Hydroxycholesterol
  - Primary bile acids
    - Chenodeoxycholic acid
    - Cholic acid
  - Secondary bile acids
    - Deoxycholic acid
    - Lithocholic acid
    - Ursodeoxycholic acid
Fat-soluble vitamins and waxes

• Fat-soluble vitamins are
  – Vitamin A
  – Vitamin D
  – Vitamin E
  – Vitamin K

• Waxes are esters of long chain fatty acids and high molecular weight alcohols
Types of lipids (recap)

- Individual fatty acids
- Triglycerides
- Phospholipids
- Sphingolipids
- Glycolipids
- Cerebrosides
- Cholesterol and related steroids
- Fat-soluble vitamins
- Waxes
Lipid digestion

- Triglycerides make up the majority of dietary lipids
- Their breakdown is facilitated by pancreatic lipases in the intestinal tract.
- This process is hugely facilitated by the emulsifying action of lecithin-rich bile acids and salts.
- The product is two free fatty acids and a 2-monoglyceride – i.e. the residual FA sits on the second C atom
- Inside the enterocytes the TGs are rebuilt and packaged with cholesterol into chylomicrons
Lipoproteins

• So far we have covered individual lipids
• The next stage is to consider their metabolism and functions
• TGs are absorbed as chylomicrons
• Then converted into more manageable forms
Chylomicron composition and function

• Composition
  – Lipids 99%
    • TGs 85-92%
    • Phospholipids 6-12%
    • Cholesterol 1-3%
  – Proteins 1-2%

• Function
  – Transport lipids from S.I. to target organs
  – Hydrolysed by lipoprotein lipase to release FAs
  – Fats delivered to target tissues
  – After loss of significant TGs, the remnant goes to the liver
VLDL composition

- Lipids 91%
  - TGs 55% of lipids
  - Cholesterol 25%
  - Phospholipids 20%
- Proteins 9% (mostly apoproteins, the non prosthetic group part of active enzymes)

Very Low Density Lipoproteins (VLDL)

In the liver:
the TGs, from chylomicrons,
plus locally synthesised TGs,
plus other components, including new proteins,
are packaged into the less dense VLDLs
These travel through the peripheral capillaries,
lipoprotein lipase catalyses removal of FA
FAs are delivered to target tissues
VLDLs become Intermediate Density Lipoproteins (IDL)

Intermediate density lipoproteins (IDL)

When IDLs reach the liver,
additional triglycerides are removed,
the IDLs become LDLs
(with less TG content the density increases)
the proteins are altered,
LDLs circulate and cholesterol is delivered to target tissues - that need it for the roles listed earlier
Low Density Lipoproteins (LDLs)

• Structure
  – Lipids  80%
    TGs      10% of lipids
    Cholesterol  50%
    Phospholipids 20%
  – Protein  20%

• Function
  – Deliver cholesterol to appropriate tissues

• Problems
  – High levels can
    • Perpetuate circulating fat-soluble toxins
    • Be indicative of possible blockage of conversion to HDLs
LDLs deliver cholesterol

- LDLs leave the bloodstream through capillary pores.
- Once in peripheral tissues, the LDLs are absorbed by the tissue cells.
- The amino acids and cholesterol enter the cytoplasm.
- The cholesterol is used:
  - For the synthesis of other steroid lipids
  - As a component of cell membranes
- Unused cholesterol diffuses out of the cells

(Martini 2004)
High Density Lipoproteins (HDL)

- Structure
  - Lipids 44%
    - TGs 6%
    - Cholesterol 47%
    - Phospholipids 46%
  - Protein 56%
  - The smallest and most dense of the lipoproteins
High Density Lipoproteins (HDL)

• Function
  – Can pick up ‘spent’ cholesterol released into the blood stream by tissues
  – Lecithin-cholesterol acyltransferase (LCAT) facilitates this
  – Cholesterol-rich HDL returns to the liver
  – Much of this cholesterol is made into and excreted as bile acids and bile salts.
  – HDLs having ‘given up’ their cholesterol are released into the blood stream and free to re-circulate and repeat the process
HDL Protective Functions

- HDL can pick up cholesterol from atherosclerotic arteries
- Anti-inflammatory
- Anti-oxidant
- Anti-coagulation
- Inhibits platelet aggregation
- Low levels of HDL are associated with poor memory

Lipoproteins - overview
[image online] available at http://courses.washington.edu/conj/bess/cholesterol/liver.html
Fatty acid transport into the cells

- Lipids are delivered to cells as Fatty Acids
- They cross the cell membrane, traverse the cytosol and reach the mitochondria
- Carnitine, A dipeptide
  - synthesised from lysine and methionine, facilitates transport of the fatty acids across the cell membrane and the mitochondrial membrane
  - Carnitine deficiency can reduce lipid use for energy increase adipocyte storage and weight gain

Fatty acid catabolism – 3 steps

   • The FA is broken down to 2-C molecules: as acetyl CoA. These enter the citric acid cycle, as do the acetyl CoA groups from glucose catabolism

2. Acetyl CoA groups are oxidised, via the citric acid cycle, to CO₂ and H₂O

3. The electron transport chain converts NADH, FAD etc. to ATP, the ‘currency’ needed by energy-requiring reactions.
Regulation of lipid metabolism

Lipolysis is stimulated by:

- Epinephrine, norepinephrine,
- Adrenocorticotropic hormone (ACTH)
- Thyroid-stimulating hormone (TSH), thyroxine
- Glucagon
- Growth hormone

Insulin antagonizes the lipolytic effects of these hormones

(Gropper et al 2005)
Glucose for short term energy

• To fulfil short-term energy demands, cells metabolise the circulating blood glucose
• Some (approximately 5%) of this is released in the cytosol
• The rest, (approximately 95%) is released in the mitochondria via the citric acid cycle and the electron transport chain
• Longer term energy will come from lipids
Longer term energy from lipids

- Lipid droplets in cells are large and can be difficult to access by water-soluble enzymes
- Fatty acids are catabolised by beta-oxidation in the mitochondria, to acetyl CoA groups
- The acetyl CoA is further catabolised in the citric acid cycle
- Mitochondria activity is limited by the availability of O2
- Lipids provide the greater energy per 1g (approximately 9 calories) compared to carbohydrates (approximately 4 calories)
- Lipid catabolism is inhibited if mitochondrial function is poor
Synthesis of Triglycerides

- TGs are the main form of dietary fat and
- TGs are also main form of stored adipose fat
- TG synthesis involves esterification of 3 fatty acids to a glycerol backbone
- Remember: an ester is a combination of an alcohol group with an organic acid
- TG synthesis occurs whenever caloric intake exceeds energy requirements
- This excess intake can come from carbohydrate, fat or protein
- Synthesis takes place predominantly in adipose tissue and liver
- It also occurs in the mammary gland during lactation
Utilisation of Triglycerides

• Adipocytes are supplied by extensive network of blood vessels
• They acquire TGs from circulating lipoproteins, chylomicrons and VLDLs
• Lipoprotein lipase releases free fatty acids and glycerol
• When lipids are needed for energy or metabolism:
  – TGs are mobilised from adipocytes facilitated by an enzyme, hormone-sensitive lipase, and released into the bloodstream
Fatty acid synthesis

- Fatty acids are synthesised from acetylCoA sequentially until palmitic acid (C16) is reached.
- Acetyl-CoA is created in the breakdown of carbohydrates.
- If there is excess glycolysis and so excess production of acetylCoA, this can be used to synthesise fatty acids.
- This is done in the mitochondria.
- i.e. excess carbohydrate consumption leads to increased fatty acid production.
- TGs are formed by the combination of 3 fatty acids and 1 molecule of glycerol.
Fatty Acids Synthesis – cont:

Diet may regulate fatty acid synthesis:

• Fatty acid oxidation and synthesis requires a number of vitamins: B2, B3, B5, biotin etc.
• The ratio of fats:proteins:carbohydrates in the diet affects hormones that regulate fatty acids synthesis
• Fatty acid synthesis increases when people switch from high-fat to high-carbohydrate diet
• However in humans de-novo fatty acid biosynthesis is relatively low, even in high-carbohydrate diets

(Garrow et al 2004; Geissler and Powers 2005; Rolfest et al 2006)
Fatty acid inter-conversions

- Many dietary fatty acids have to be changed into different fatty acids for normal cellular function
- 2 processes are common:
  - Elongation: a process whereby a 2-carbon acetyl group is added and increases the chain length by 2
    - This is catalysed by elongases
  - Desaturation: a process by which 2 hydrogen atoms are removed, creating a residual double bond
    - This is catalysed by desaturases
- The two processes generally occur alternately
- Several coenzymes are required: B6, Mg, Zn, Mn
Fatty acid elongation and desaturation
Carbohydrate – lipid relationships

Regulation of Lipid Metabolism

**Hyperglycaemia** → insulin release → promotes glucose transport to cells → lipogenesis facilitated

**Hypoglycaemia** → low levels of insulin
  → promotes lipolysis
  → lipogenesis inhibited

stimulation of fatty acid oxidation

(Gropper et al 2005)
Ketone synthesis

Ketones are released in starvation, diabetes mellitus, low carbohydrate diet. These lead to:

→ low carbohydrate levels
→ low glucose levels
→ low rate of glycolysis
→ low levels of 4-carbon units oxaloacetate (OxAc) essential for first step into the Citric Acid Cycle
→ the Citric Acid Cycle is inhibited
→ there is increased oxidation of FAs for energy
→ accumulation of Acetyl CoA
→ increased ketone (3 types) formation.

(Gropper et al 2005)
Ketosis

- These reactions lead to an accumulation of ketones
- Ketones are lost in the urine can be detected in the urine by a simple test give the urine a ‘pear drop’ smell
- These ketones retain the majority of the energy derived from carbohydrates and lipids.
- Hence this strategy lay behind weight-loss diets such as the “60 gm(of carbohydrate) diet”, the Atkins diet” and similar titles
- Ketosis is dangerous, stresses the kidneys and disturbs body acid base balance
- However it is essential in periods of starvation: the liver deliversketones to peripheral tissues like brain and muscle to provide fuel

(Gropper et al 2005)
Food sources of lipids - SFA

Common dietary saturated fatty acids:
Myristic: coconut oil, butter
Palmitic: palm oil, butter, salmon, egg yolks, beef
Stearic: beef, butter, egg yolks
# Types and Sources of Saturated Fatty Acids

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<th>Name of Acid</th>
<th>Occurrence in Foods</th>
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<td>Priopronic</td>
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<td>Butyric</td>
<td>2.5-5.4% in cow butter</td>
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<td>Valeric</td>
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<td>Caproic</td>
<td>1-2% in cow butter, trace in palm oil</td>
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<tr>
<td>Caprylic</td>
<td>1-2% in cow butter, 6-8% in cocoa butter</td>
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<td>Capric</td>
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<tr>
<td>Lauric</td>
<td>Coconut oil, cow butter and palm oil</td>
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<table>
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<th>Name of Acid</th>
<th>Occurrence in Foods</th>
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<tr>
<td>Myristic</td>
<td>milk and some vegetable fat, palm oil</td>
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<tr>
<td>Palmitic</td>
<td>almost all natural fats</td>
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<td>Stearic</td>
<td>fats of land animals</td>
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<tr>
<td>Arachidic</td>
<td>ground nut oil (3%), traces widely distributed</td>
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<td>Behenic</td>
<td>2% in ground nut and rapeseed oil</td>
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<tr>
<td>Lignoceric</td>
<td>ground nut and rapeseed oil-under 3%</td>
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<tr>
<td>Cerotic</td>
<td>traces in most vegetable fats</td>
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Food sources of lipids – monounsaturated FA

Oleic Acid - 18:1 n-9
The main fat present in: safflower oil, olive oil, rape seed oil, hazelnut oil, avocado
Also present in: most seeds, cereal, other vegetable oils
Common polyunsaturated fatty acids

- Linoleic acid (LA)  essential in the diet
- α-linolenic acid (ALA) essential in the diet
- Arachidonic acid (AA)
- Gamma linolenic acid (GLA)
- Eicosapentaenoic acid (EPA)
- Docosahexaenoic acid (DHA)
Sources of individual PUFAs

Linoleic acid (LA) 18-2 n-6 (Omega 6)
- safflower oil, sunflower seeds and oil
- abundant in most plants and vegetable oils
α-linolenic acid (ALA) 18:3 n-3 (Omega 3)

Flaxseed, hemp, canola seed, soybean, and walnut oils and in dark green leaves

• Most edible plants produce this 18-carbon polyunsaturated fatty acid
Fats-Sources

Gamma linolenic acid (GLA)  18:3 n-6 (Omega 6)

- Main food sources: evening primrose oil (EPO), blackcurrant seed oil, hemp and borage oils
Fats-Sources

PUFA

Eicosapentaenoic acid (EPA) 20:5 n-3 (Omega 3)

- Main food sources: fish, human breast milk
Lecithin - Sources

Phospholipids-Food Sources

- The richest food sources of lecithin are eggs, liver, soybeans, wheat germ, peanuts, spinach, legumes
Foods do not consist of ONE type of fat

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<tr>
<th>Vegetable Oil</th>
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What do EFA do?

- There are 2 EFA: linoleic acid and alpha-linolenic acid
- It is time to discover what they do and why they are important
Eicosanoids

- Eicosanoids made by oxidation of C20 FAs
- They are derived from either omega-3 or omega-6 FAs
- They are signalling molecules and control many functions
  - Immune function
  - Inflammation
    - Eicosanoids derived from omega-3 FAs tend to be anti-inflammatory
    - Those from omega-6 FAs tend to be pro-inflammatory
  - Blood characteristics (such as clotting)
    - Eicosanoids derived from omega-3 FAs tend to be anti-clotting
    - Those from omega-6 FAs tend to be pro-clotting
  - Neurological messenger molecules
Eicosanoid sub groups

• There are many sub groups of eicosanoids:
  – Prostaglandins
  – Prostacyclins
  – Thromboxananes
  – Leukotrienes

• They are all derived from the EFAs
  – Omega-6 and
  – Omega-3
Eicosanoid Functions

They can be thought of as being similar to micro hormones except that they are produced locally, act locally and have a very much shorter life-span.

Thus they maintain micro control, or fine-tuning, over many body functions.

They are involved in:

• Regulation of blood vessel permeability and contraction
• Blood coagulation and blood vessel integrity
• Lipid accumulation
• Immune cell behaviour
• Inflammation
• Central nervous system signalling
Essential Fatty Acids in Human Health

Gamma Linolenic Acid-GLA

[Diagram showing the metabolic pathway of Gamma Linolenic Acid (GLA) and its conversion to Arachidonic Acid]
Essential Fatty Acids-Metabolism

Inhibited by:
- Mg deficiency
- Zinc deficiency
- Insulin resistance
- Vitamin B₆ deficiency
- Refined sugars
- High intake of MUFA, SFA, TFA
- Cholesterol
- Alcohol
- Adrenaline and glucocorticoids

Inhibited by:
- Insulin resistance
- High intake of MUFA, SFA, TFA
- Cholesterol
- Zinc deficiency
- Alcohol
- Adrenaline and glucocorticoids
Essential Fatty Acids Metabolism

Diet

Omega 6 Family
- 18:2n-6
  - linoleic acid (LA)
- 18:3n-6
  - gamma linolenic acid (GLA)
- 20:3n-6
  - dihomogamma linolenic acid (DGLA)
- 20:4n-6
  - arachidonic acid (AA)
  - 22:4n-6
    - docosatetraenoic acid
  - 24:4n-6
  - C24:5n-6
  - C22:5n-6
    - docosapentaenoic acid

Omega 3 Family
- 18:3n-3
  - alpha linolenic acid (ALA)
- 18:4n-3
  - octadecatetraenoic acid
- 20:4n-3
  - eicosatetraenoic acid
- 20:5n-3
  - eicosapentaenoic acid (EPA)
  - 22:5n-3
    - docosapentaenoic acid
  - 24:5n-3
    - delta4-desaturase
  - 24:6n-3
  - C22:6n-3
    - docosahexaenoic acid (DHA)

Enzymes
- delta6-desaturase
- elongase
Essential Fatty Acids-Functions

- EFA are essential components of cell membrane
- EFA help maintain membrane fluidity
- Necessary for cell-to-cell communication (membrane enzyme activity increases with the degree of membrane lipid unsaturation)
- They act with membrane proteins thus affecting the transport of substances into and out of the cell
- EFA (ALA, DHA, AA) are essential for foetal brain development
- Remember: EFA are the precursors of eicosanoids

(Mead 1984; Crawford et al 1976; Garrow et al 2004)
There are three groups of eiconsanoids

- They derive from:
  - Dihomo-γ-linolenic acid (DGLA);
  - Arachidonic Acid (AA) and
  - Eicosapentanoic Acid (EPA)

- They lead to the production of:
  - Series 1, 2, 3 prostaglandins
  - Thromboxanes
  - Leukotrienes
Essential Fatty Acids in Human Health

EFA Imbalance

- Imbalances or deficiency in EFA and eicosanoids can contribute to many diseases characterised by low-grade systemic inflammation
  - Atherosclerosis
  - Metabolic syndrome
  - Alzheimer’s disease
  - Diabetes mellitus
  - Hypertension
  - Cancer
  - Depression
  - Schizophrenia
  - Collagen vascular diseases

(Lord and Bralley 2008; Das 2008)
Eicosanoids - Prostaglandins

Eicosanoids

3 classes: prostaglandins, thromboxanes, prostacyclins

- Prostaglandins Series 1: made from Dihomo-γ-linolenic acid (DGLA)
- Prostaglandins Series 2: made from Arachidonic Acid (AA)
- Prostaglandins Series 3: made from Eicosapentaenoic Acid (EPA)

(Lord and Bralley 2008; Garrow et al 2004)
**Eicosanoids**

The release of fatty acids from the membrane phospholipids is necessary for the formation of eicosanoids

- The releasing enzyme - **phospholipase**

(Lord and Bralley 2008)
Essential Fatty Acids-Metabolism

Eicosanoids

- Fatty acid membrane composition determines which prostaglandins will predominate
- Membrane composition is determined by the diet and the desaturation/elongation reactions
- More AA, LA in the diet - more PGE2; more ALA/EPA in the diet - more PGE3, more GLA in the diet - more PGE1

(Lord and Bralley 2008)
Prostaglandin Series 1 (PGE1)

- Moderately anti-coagulant, reduce risk of heart attacks, strokes
- Help to remove sodium and water excess from the body
- Relax blood vessels improving circulation, lowering blood pressure, relieving angina
- Moderately anti-inflammatory and therefore balance some of the inflammatory prostaglandins
- Prevent the release of Arachidonic Acid (precursor of proinflammatory PGE2) from the cell membranes

(Lord and Bralley 2008; Erasmus 1993)
Prostaglandin Series 2 (PGE2)

- Some prevent, some promote platelet aggregation (clot formation)
- Promote sodium and water retention
- Promote inflammation
- PGE 2 oppose the functions of PGE1

(Lord and Bralley 2008; Erasmus 1993)
Prostaglandin Series 3 (PGE 3)

- Some of PGE3 have weak platelet aggregating properties
- Most powerful effect of PGE3 is the fact that EPA, their parent substance, prevents AA from being released from membranes-preventing PGE2 from being made
- EPA is the most important factor in limiting PGE2 production

(Lord and Bralley 2008; Erasmus 1993)
Prostaglandin Pathways

Fortier et al (2008) Fig. 1. Prostaglandin biosynthesis pathways [online image] Available at http://www.jpp.krakow.pl/journal/archive/08_08_s1/articles/03_article.html
EFA balance

- Today’s Western diet is:
  - Abundant in omega-6: LA (most plant oils), AA (meat, dairy)
    - Hence high in PG2 series activity
  - Low in omega 3: ALA (flaxseed, pumpkin seeds) and EPA, DHA (fish)
    - Hence low in PG1 and PG3 series activity
    - Promotes hyperlipidaemia and insulin resistance
  - High in total fat
  - Often low in B6, Mg, Zn and Mn – needed for EFA metabolism
  - Hence correct eicosanoid function can be compromised

(Lord and Bralley 2008; Das 2008; Garrow et al 2004)
Essential Fatty Acids—Metabolism

- Fatty acids can be modified by:
  - **Desaturation enzymes** - that introduce double bonds
  - **Elongation reactions** - that add 2-carbon units to the carboxyl (–COOH) end

- **Desaturation** and **elongation** produces families of fatty acids derived from the common precursor: **Linoleic acid (LA)** and **Alpha Linolenic Acid (ALA)**

- Therefore only **ALA and LA** are considered **dietary EFAs**

(Lord and Bralley 2008)
Delta-6 Desaturase:

This enzyme is inhibited by

- Mg and zinc deficiency
- insulin resistance
- Vitamin B₆ deficiency
- diet high in refined sugars
- high intake of monounsaturated, saturated and trans fatty acids!
- cholesterol
- alcohol
- adrenaline and glucocorticoids

(Lord and Bralley 2008; Das 2006; Das 2006a)
Essential Fatty Acids-Metabolism

Delta-5 Desaturase:

Is inhibited by:

- Insulin resistance
- High intake of monounsaturated, saturated and trans fatty acids!
- Cholesterol
- Alcohol
- Inadequate zinc
- Adrenaline and glucocorticoids

(Lord and Bralley 2008; Das 2006; Das 2006a)
Essential Fatty Acids-Metabolism

Therefore impact of EFA supplementation will be limited if the patient:

- Has low Zn status
- Has low Mg status
- Has hyperinsulinaemia (linked to high fat, high refined carb diet)
- Consumes excess of fats - MUFA, SFA, TFA
- Has hyperlipidamia, diabetes, hypertension

- Thus **QUANTITY** and **QUALITY** of dietary fats and the **whole diet** important!
- **Do not just supplement, correct metabolic abnormalities with the diet first.**

(Lord and Bralley 2008; Das 2006; Das 2006a)
Essential Fatty Acid conversions

DHA-EPA conversion:

• Most fatty acid conversions take place in endoplasmic reticulum
• Conversion of EPA to DHA requires additional enzymes that are present only in peroxisomes

• Because of the passage between organelles the rate of conversion of ALA to DHA is much slower than the ALA-EPA conversion

(Lord and Bralley 2008)
Eicosanoid Metabolism

(Lord and Bralley 2008)
AA metabolites and Inflammation

(Kumar 2005)
Essential Fatty Acids in Human Health

Alpha Linolenic Acid (Omega 3)

Popular Uses

- Hypertension
- Heart disease
- Rheumatoid arthritis (RA)
- Multiple sclerosis (MS)
- Lupus
- Diabetes
- Hypercholesterolemia
- Renal disease

- Chronic obstructive pulmonary disease
- Migraine headache
- Skin cancer
- Depression
- Psoriasis
- Eczema
- Ulcerative colitis and Crohn's disease

(Garrow et al. 2004)
Essential Fatty Acids in Human Health

ALA Potential Clinical Applications

• Arthritis
• Depression
• Inflammatory Bowel Diseases
• Asthma

• ALA might be beneficial in these conditions, there is lack of scientific consensus in this area, results from trials have been varied but many positives – more research needed
• Research was conducted predominantly with dietary or supplemental EPA

(Ortega et al 2012; UMMC 2002)
Essential Fatty Acids in Human Health

ALA: Evidence-Based Efficacy

Cardiovascular Disease

• Dietary ALA decreases the risk of primary and secondary heart attack
• Dietary ALA reduces calcified atherosclerotic plaque in the coronary arteries
• ALA reduces C-reactive protein levels, but does not influence lipid profiles (LA influences lipid profiles)

Hypertension

• Trials suggest dietary ALA reduces hypertension

Essential Fatty Acids in Human Health

Adverse Reactions/Toxicity

Prostate Cancer
- There is substantial evidence that excess ALA can increase the risk of prostate cancer and advanced prostate cancer.

Obesity
- ALA is high in calories, if consumed in excess may contribute to weight gain.
- Patients should be advised to reduce their intake of other fats when adding ALA to their diet and not to consume them additionally to their current fat consumption.

(Leitzman et al 2004; Ramon et al 2000; Brouwer et al 2004; Pedersen et al 2000)
Essential Fatty Acids in Human Health

Adverse Reactions/Toxicity

Heart Disease

- Avoid the use of margarine as a source of alpha-linolenic acid
- Margarine can contain high concentrations of trans-fatty acids. These can increase the risk of heart disease and myocardial infarction

Hyper triglyceridaemia

- Excess ALA might increase triglyceride levels and potentially worsen hypertriglyceridaemia

( Pedersen et al 2000; Finnegan et al 2003)
Essential Fatty Acids in Human Health

ALA Drug Interactions

- **Blood-thinning Medications**
  
  Omega-3 fatty acids may increase the blood-thinning effects of warfarin, aspirin, or other blood-thinning medications.

- While the combination of aspirin and omega-3 fatty acids may actually be helpful under certain circumstances (such as heart disease), these medications should only be taken together under the guidance and supervision of GP

(UMMC 2002)
ALA Drug Interactions

• Cholesterol-lowering Medications

Increasing the amount of omega-3 fatty acids in your diet and reducing the omega-6 to omega-3 ratio, may allow a group of cholesterol lowering medications known as "statins" (such as atorvastatin, lovastatin, and simvastatin) to work more effectively.

(UMMC 2002)

– A high fibre diet will help to increase the excretion of cholesterol (from bile acids and pigments) in the stool
Essential Fatty Acids in Human Health

GLA Popular Uses

- Rheumatoid arthritis
- Hyperlipidemia
- Heart disease
- Syndrome-X
- Diabetic neuropathy
- Cancer prevention
- Attention deficit-hyperactivity disorder (ADHD)

- Chronic fatigue syndrome
- Allergic rhinitis
- Psoriasis
- Eczema
- Depression
Essential Fatty Acids in Human Health

GLA Potential Clinical Applications

Rheumatoid Arthritis (RA)

- GLA can be converted to compounds that have anti-inflammatory properties – and can act on NF-kappaB and AP-1
- Some research suggests that GLA might act directly on T-cells to modulate immune response in diseases such as rheumatoid arthritis (RA)
- Supplementation with GLA and EPA may diminish joint pain, swelling, and morning stiffness

(Chang et al 2010; Fan and Chapkin 1998; Leventhal et al 1993; Darlington et al 2001; Kast 2001)
Essential Fatty Acids in Human Health

GLA Potential Clinical Applications

Attention Deficit/Hyperactivity Disorder (ADHD)

- Research to date has suggested an improvement in symptoms and behaviors related to ADHD from omega-3 fatty acids
- Results of studies supplying omega-6 fatty acids in the form of GLA from EPO or other sources to children with ADHD, however, have been mixed and inconclusive
- A recent meta-analysis has indicated GLA and EPA had the most potential for positive impact

(Burgess 2000; Puri and Martins 2014; Richardson and Puri 2000)
GLA Potential Clinical Applications

Menopausal Syndromes

- Although EPO has gained some popularity for treating hot flashes, the research to date **has not yet demonstrated** a benefit of GLA or EPO over taking a placebo

- However, there are individual women who report improvement

(Chenoy et al 1994)
Although results of studies have been mixed, some women find relief of their PMS symptoms when using GLA supplements from EPO or other sources. The symptoms that seem to be helped the most are breast tenderness and feelings of depression as well as irritability and swelling and bloating from fluid retention. Breast tenderness from causes other than PMS may also improve with use of GLA.

(Horrobin et al 1983; Bendich 2000)
Essential Fatty Acids in Human Health

GLA Potential Clinical Applications

Eczema

• Several early studies suggested that EPO (rich in GLA) is more beneficial than placebo at relieving symptoms associated with this skin condition such as redness, scaling and most noticeably itching.

• Whether EPO and GLA supplements work for someone with eczema may be very individual.

(Morse et al 1989; Worm et al 2000)
GLA Potential Clinical Applications

Allergies

• GLA has a longstanding history of folk use for allergies

• To date, the use of EFA (GLA) to prevent allergic reactions or reduce their magnitude has had mixed results

• Whether this supplement improves your symptoms, therefore, may be very individual.

(Calder et al 2000; Kankaanpaa et al 2001)
Essential Fatty Acids in Human Health

GLA  Evidence-Based Efficacy

Diabetic Neuropathy

• Taking GLA orally for 6 months to 1 year reduces symptoms and prevents neurological deterioration in neuropathy patients who have type 1 or type 2 diabetes

• It seems to be more effective in patients with better glucose control compared to patients with poor glucose control

Borage seed oil, and possibly other sources of GLA, should not be used during pregnancy. There is little known about the possible consequences of GLA supplementation during pregnancy and it is best to err on the side of caution.

- Dosages of GLA greater than 3,000 mg per day should be avoided because, at that point, production of AA (rather than DGLA) may increase.
Essential Fatty Acids in Human Health

GLA Drug Interactions

- **Ceftazidime** - GLA may increase the effectiveness of ceftazidime, an antibiotic in a class known as cephalosporins, against a variety of bacterial infections.

- **Chemotherapy for cancer** - GLA may increase the effects of anti-cancer treatments, such as doxorubicin, cisplatin, carboplatin, idarubicin, mitoxantrone, tamoxifen, vincristine, and vinblastine.

- **Cyclosporine** - taking omega-6 fatty acids, such as GLA, during therapy with cyclosporine, a medication used to suppress the immune system after an organ transplant, for example, may increase the immunosuppressive effects of this medication.

(UMMC 2002)
GLA Drug Interactions

• **Nonsteroidal Anti-inflammatory Drugs (NSAIDs)** — the use of NSAIDs, such as ibuprofen, together with borage oil or other GLA containing supplements may counteract the effects of the supplement.

**Phenothiazines for schizophrenia** - individuals taking a class of medications called phenothiazines (such as chlorpromazine, fluphenazine, perphenazine, promazine, and thioridazine) to treat schizophrenia should not take EPO because it may interact with these medications and increase the risk of seizures. The same may be true for other GLA containing supplements.

(UMMC 2002)
Essential Fatty Acids in Human Health

Supplementation/Dietary Dosage

• The recommended dosage for *rheumatoid arthritis* is 1,400 mg per day of GLA or 3,000 mg of EPO

• For *diabetic neuropathy* it is 480 mg per day of GLA

• For *breast tenderness* or other symptoms of PMS, 3,000 to 4,000 mg of EPO per day is the dose suggested

• For other conditions discussed, a specific safe and appropriate dose of GLA supplements has not yet been established

• Studies have suggested that up to 2,800 mg of GLA per day is well tolerated (UMMC 2002)
Essential Fatty Acids in Human Health

**Fish Oils**: Eicosapentaenoic Acid –EPA and Docosahexaenoic Acid- DHA
Essential Fatty Acids in Human Health

EPA Popular indications for use

- Depression
- Hypertension
- Coronary artery disease
- Schizophrenia
- Alzheimer’s disease
- Diabetes
- Cystic fibrosis

(Garrow et al 2004)
Essential Fatty Acids in Human Health

EPA /DHA Combination popular indications for use

• Asthma
• Heart disease
• Cancer
• Eczema
• Depression
• Autoimmune conditions
• Hayfever
Essential Fatty Acids in Human Health

Potential Clinical Applications

– Arthritis

• The omega-3 fatty acids found in fish oils have been shown to modify the immune response and may be helpful in treating inflammatory autoimmune diseases such as rheumatoid arthritis.

• Supplementation with GLA and fish oils may diminish joint pain, swelling, and morning stiffness

(Danao-Camara 1999; UMMC 2002; Kremer 2000)
Essential Fatty Acids in Human Health

Potential Clinical Applications

– Attention deficit-hyperactivity disorder (ADHD)

• Some research shows that low plasma levels of EPA and other omega 3 fatty acids are associated with ADHD in children

• Some studies have shown positive effect of fish oil supplementation in children with ADHD; however, intervention studies using EFAs to treat behavioral problems have reported varying results.

• It is not known if fish oil supplements can treat or prevent ADHD; relatively few studies support EFA effectiveness for ADHD

(Stevens et al 1995; Burgess et al 2000; Richardson and Puri 2000; UMMC 2002)
Essential Fatty Acids in Human Health

Evidence-Based Efficacy

- Heart Disease/Hypertension

  • Omega-3 fatty acids have been shown to improve cardiovascular health and may prevent the accumulation of plaque (cholesterol and fat) on the walls of the arteries

  • Fish oil supplementation may also reduce high blood pressure in people with diabetes.

(Adreassen et al 1997; Angerer et al 2000; UMMC 2002)
Evidence-Based Efficacy

- Depression

  • Dietary or supplemental fish oils with standard therapy seems to improve symptoms of recurrent major depression, such as depressed mood, guilt feelings, worthlessness, and insomnia after two weeks of treatment

(Nemets 2002; Bruinsma 2000)
Essential Fatty Acids in Human Health

Adverse Reactions/Toxicity

Supplements containing EPA may not be recommended for infants or small children because they upset the proper balance with DHA, which is needed during early development.

This suggests that pregnant women should also be cautious about taking fish oil supplements.

Make sure the fish oil supplement you use has been tested for heavy metals, such as mercury and lead.

Vitamin A in fish oil supplements along with a multivitamin (which also contains vitamin A) may cause over dosage.

(UMMC 2002)
Essential Fatty Acids in Human Health

Adverse Reactions/Toxicity

Fish oil capsules may be associated with side effects like **loose stools**, abdominal discomfort, and unpleasant belching.

They **may prolong bleeding time**; doses **greater than 3 grams** daily might decrease blood coagulation and increase the risk of bleeding.

Consumption of fish oil supplements may **also increase antioxidant requirements in the body**.

- Taking extra vitamin E along with these supplements may be warranted, (UMMC 2002)
Supplementation/Dietary Dosage

The International Society for the Study of Fatty Acids and Lipids (ISSFAL) recommends the following intakes of EPA:

- The adequate daily intake of EPA for adults should be at least 220 mg per day.
- Therapeutic recommendations from diet: 2 - 3 servings of fatty fish per week, which corresponds to 1,250 mg EPA plus DHA per day.
- Fish oil supplements: 3,000 - 4,000 mg standardized fish oils per day. This amount corresponds to 2 - 3 servings of fatty fish per week.

(UMMC 2002)

Decreasing the amount of omega 6 from convenience foods, fast foods, cakes and margarines based on sunflower or safflower oil and can improve your ratio of EFAs.

(Brewer, 2010)
Essential Fatty Acids in Human Health

EPA/DHA Drug Interactions

Blood Pressure Medication - DHA may lower blood pressure, so it could make the effects of prescription blood pressure medication stronger.

Anticoagulants (blood thinners) - EPA in fish oil supplements may increase bleeding time, so fish oil could make the effects of these drugs stronger. The same does not appear to be true of DHA alone.

Diabetes medications - fish oil supplements may lower levels of glucose in the blood and could make effects of diabetes drugs stronger.

Aspirin - in combination with aspirin, fish oil could be helpful in the treatment of some forms of coronary artery disease. However, this combination may also increase the risk of bleeding.

(UMMC 2002)
Fats-Sources

Reading: critical review of the claims of fish oils manufacturers

- Centre of Science for Public Interest

- free access cut and paste: http://www.cspinet.org/nah/10_07/cover_omega3.pdf
Essential Fatty Acids Supplementation Guidelines

Before Supplementing Address the Diet First

- Address patient’s diet:
  - Omega 6/3 ratio not more than 4:1
  - Correct Zn deficiency, combine with Mn
  - Correct vitamin B deficiency
  - Correct Mg deficiency
  - Address excess alcohol use
  - Address excess sugar intake

especially in vegetarians who do not consume fish!!
Essential Fatty Acids Supplementation Guidelines

• **EFA Guidelines for Vegetarians/Vegans:**
  
  • Include good sources of alpha-linolenic acid in the daily diet, such as flaxseed oil
  
  • Moderate the use of oils rich in omega-6 fatty acids, and high-fat processed foods rich in these oils.
  
  • Make the primary dietary fat monounsaturated, if consuming more than 15 percent of calories from fat
  
  • Consider including a direct source of EPA and/or DHA in the diet (Algae EPA/DHA supplements)

(Davis 2007)
Too much of a good thing!
The risk of excessive n-3 EFA supplementation has risen along with the awareness of its health benefits

- **n-3 dominance syndrome:**
  - Suppressed immune system (difficulty overcoming infections)
  - Increased risk of bleeding
  - Risk of toxic mercury accumulation from fish extracts
  - Risk of carcinogenic contaminants stored in adipose tissue of fish
  - Risk of oxidative damage and elevated serum lipid peroxides

Be aware of these situations so that they do not become a problem

(Lord and Bralley 2008; Bays 2007; Sidhu 2003)
High or low fat diet

- Over recent decades there have been arguments for a high fat diet and arguments for a low fat diet
- Each has had its strong adherents
- There is still no overall agreement
- It is important to consider:
  - If you tell someone to eat a low fat diet, what will they eat instead?
  - It will almost certainly be a diet rich in grains, almost certainly largely refined, and sugars
  - Yet there is a growing awareness of the dangers of a high carbohydrate diet in relation to diabetes, cancer and other diseases
Good and bad oils and fats

• Many of the problems of oils and fats in the diet stem from the way they are obtained, treated and used.
• Healthy oils are
  – specially extracted flaxseed oil (store in a deep freeze to prevent oxidation),
  – coconut oil (for cooking),
  – olive oil and
  – avocado oil.
  These oils can be extracted with relatively little processing.
• So called ‘cold-pressed oils’ from hard seeds, are obtained by applying such strong pressures that sufficient heat is generated to char the residual fibrous ‘mat’, and this heat can damage the oil
• Other oils are solvent extracted using toxic solvents that then have to be removed (but are rarely 100% removed)
Overheated oils and fats

- Overheating fats leads to the formation of toxic compounds.
- Butter browns above 150°C and smokes above 200°C. Overheated butter should not be eaten.
- Overheated, smoking or burnt fats on meats can be harmful.
- Oxidised cholesterol should not be eaten.
- Experiments with it have contributed to cholesterol’s bad name.
- These are topics you should be aware of, consider and research.
High or low fat diet - cont

• Fats offer many advantages over carbohydrates:
  – Greater satiety value
  – Sources of essential fatty acids
  – Sources of essential fat-soluble vitamins and phytonutrients
• Quality of lipids
  – Arguably it is more important to consider the quality of the lipids than the quantity
  – Avoid:
    • Overheated fats, burning or smoking fats
    • Rancid fats including rancid or oxidised vegetable oils
      (The more unsaturated the fatty acid the more it is vulnerable to oxidation)
    • Oxidised cholesterol
    • Trans fatty acids, hydrogenated or hardened fats and spreads
    • Mineral oils – they leach fat-soluble nutrients from the body
Saturated fats...?

• A question mark hangs over saturated fats and heart disease. Dr Malhotra a cardiologist from a London hospital challenges the role of saturated fats and cardiovascular risk.

• Read more – cut and paste the below links:
  - [http://www.bmj.com/content/347/bmj.f6340](http://www.bmj.com/content/347/bmj.f6340)
Recommended intakes of lipids

Official recommended intakes of fat: **15-30% of dietary energy (WHO)**; mostly from PUFA and MUFA fat sources like vegetable oils, nuts, seeds, fish

- Linoleic Acid: 5-10% of energy intake
- Linolenic Acid: 0.6-1.2% of energy intake
- Saturated fats: max. 7% of energy intake
- Trans fats: max. 1% of energy intake
- Dietary cholesterol: max. 300mg/day

(Rolfes et al 2006; American Heart Association 2008)
Fat Requirements

In theory humans need to obtain only essential fatty acids (EFA) from the diet, as all other fats can be synthesized in the human body.

There is no consensus as to the actual levels of human EFA needs. The recommendations vary between 3-11% of total energy.

- **International Society for the Study of Fatty Acids and Lipids:**
  - Linoleic Acid LA -2%
  - Alpha Linolenic Acid ALA -0.7%
  - A healthy **upper limit** of the intake of LA -3%!

(Hurley 1984; Gawecki 2008; ISSFAL 2008)
Consequence of excess or inadequate lipid intake

Heart Disease/Stroke-Beneficial Effect of Unsaturated fats

- **MUFA** when substituted for SFA lower cholesterol
- **Omega-6 PUFA** lower LDL and HDL cholesterol when substituted for SFA
- **Omega-3 PUFA** have little effect on LDL cholesterol, rather they reduce the triglycerol concentrations, decrease the platelet aggregation and blood pressure and may raise HDL cholesterol

(Schaefer 2002; Mensink and Katan 1992; Valsta et al 1992; Rolfes et al 2006; Garrow et al 2004; PCRM 2006)
Ideal Fat Intakes - Types of Fat

- It is estimated that throughout human evolution:

  The ratio between Omega 6 and Omega 3 EFA was much lower (1 as opposed to today’s 11-15)

- The ratio of Omega 6 to Omega 3 EFA should be between 3-1:1, as opposed to 15:1

- This ratio ensures maximal conversion to both EPA and DHA

- This corresponds to **5-8 percent** of calories from Omega 6PUFA and **1.25-2.5%** of calories from Omega 3 PUFA

  (Simopolous 2000; Jenkins et al 2006, Hurley 1984; Masters 1996)
Ideal Fat Intakes - Practicalities

American Institute for Cancer Research Guidelines

- Choose mostly plant foods
- Aim for meals made up of **2/3 (or more)** vegetables, fruits whole grains or beans and **1/3 (or less)** animal products
- Use oils in moderation, rather get your plant fats from unrefined products like seeds and nuts
- Choose adequate levels of Omega 3-rich food sources: flaxseeds, walnuts or pumpkin seeds, olives and avocados
- Replace meat with fish 2-3 times a week
- Minimize the consumption of red and processed meats
- Make it vegetarian several times a week
Balance fats and carbohydrates

A diet should be based on

- small amounts of unrefined carbohydrates:
- moderate amounts of pulses and fruits
- a large proportion of vegetables

If predominantly refined carbohydrates are consumed, it can lead to:

- High LDL cholesterol
- High triglycerides
- Low HDL cholesterol
- Diabetes

(Geissler and Powers 2006, Rolfes et al 2006)
Overall diet

• Instead of debating a high or low fat diet or
  – A high or low carbohydrate diet.
  – The focus should be on
    • a high vegetable and moderate fruit diet
    • more raw food
    • moderate amounts of good quality fats
    • very moderate amounts of carbohydrates, all of which should be unprocessed (such as whole grains) and rich in their natural phytonutrients
    • moderate amounts of good quality protein foods