Chapter 3 Carbohydrates, Proteins, and Fats and Oils: the building blocks of nutrition

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Biological significance of carbohydrates
Energy stores
Proteins
Protein metabolism
Synthesis of proteins
Biological Significance of proteins
Role of protein in body’s defense mechanisms
Fats and oils
Essential fatty acids
Intrauterine supply of PUFA
PUFA supply through human milk
Effect of PUFA on the immune system
Dietary sources of unsaturated fatty acids
Dietary fat
Fat as a source of energy
Digestion of lipids
Oxidation of fatty acids
Gut Flora

Figure 3.1 Food for the basic processes of life
Figure 3.2 Starch and glycogen compared
Figure 3.3 Relationships between utilization and storage of energy from food
Figure 3.4 Oxidation of carbohydrate to produce energy
Figure 3.5 Chemical structure of ATP (Adenosine triphosphate)
Figure 3.6 Fate of glucose
Figure 3.7 Recommended daily allowances
Figure 3.8 Synthesis of tissue proteins
Figure 3.9 Chemical structure of amino acid
Figure 3.10 Amino acids in energy metabolism
Figure 3.11 Mammalian cell
Figure 3.12 The DNA molecule
Figure 3.13 Stepwise schematic representation of protein synthesis
Figure 3.14 protein synthesis
Figure 3.15 Molecules of haemoglobin and insulin
Figure 3.16 summarizes the fate of amino acids in the body
Figure 3.17 Chemical Structures of glycerol, triglycerides and phospholipids
Figure 3.18 Saturated and unsaturated fatty acids
Figure 3.19 Typical triglycerides of vegetable animal and fish origins
Figure 3.20 The two classes of poly-unsaturated fatty acids
Figure 3.21 Carbohydrate, protein and fat in energy metabolism
Figure 3.22 Transport of very low density lipo-proteins
Table 3.1  Energy content of common foods and the number of minutes of activity needed to burn an equivalent amount. .................................................................61
Table 3.2  Energy expenditure during different activities for a 70 kg person ................................61
Table 3.3  Average daily requirements of energy, protein, vitamin A, folic acid, iron and iodine. 68
Table 3.4  Essential amino acid patterns of some common foods. (mg. of amino acid per 1g of protein). Limiting amino acids are highlighted.........................................................70
Table 3.5  Recommended levels of protein and essential amino acid intake for infants and children ........................................................................................................................................72
Table 3.6  Fatty Acid Content of some Foods ........................................................................87
Carbohydrates, fats and oils and proteins are the major constituents of the foods that we eat. Their main purpose of food is to provide energy for the basic processes of life (respiration, circulation, and metabolism), for the mechanical work performed by muscles, for growth, maintenance of body warmth, and for making good the wear and tear brought by daily activity. Body tissues are in a dynamic state of breaking down (catabolism), and regeneration (anabolism). Foods consumed in our daily diet supply the essential raw materials for growth and repair as well as the energy needed for the chemical reactions involved. In this respect carbohydrates, fats and proteins can be interchanged as sources of energy. (see Fig. 3.1). Adenosine triphosphate (ATP) is a versatile source of energy. It can be generated by oxidizing several metabolic fuels, although carbohydrates and fats are especially important for the purpose. ATP is used in innumerable metabolic reactions and physiological functions in all forms of life, including humans. The primary objective of metabolism is to maintain a steady supply of ATP as readily utilisable energy source for normal everyday processes of life.

Carbohydrates are widely distributed in both plant and animal tissues. In plants they are produced by photosynthesis and include the cellulose of the plant framework as well as the starch in the plant cells. Starch is the important food source of carbohydrate and is found in cereals, potatoes, legumes and other vegetables. Glycogen is often referred to as animal starch, and is the polysaccharide of animal tissues. The structures of starch and glycogen are compared in Figs. 3.2.

Figure 3.1 Food for the basic processes of life
Both starch and glycogen are long-chain polysaccharides formed of units joined together by glycosidic bonds. As seen in Figure 3.2 glycogen is a polymer of glucose molecules which form a branched spherical structure. Its very large molecular weight enables glucose to be stored without causing osmotic overload which would be the case with same number of free glucose molecules. The size of the glycogen molecule varies with the nutritional status of the host, being larger in the fed state and progressively getting smaller in between meals. The three most common products of carbohydrate digestion are glucose, galactose and fructose. Carbohydrate–rich cereals compare favourably with protein–rich foods in energy value. They also contribute protein of vegetable origin. Since cereals are significantly less expensive to produce most of the world’s diets are arranged to meet main caloric requirements from carbohydrate foods, and protein – rich foods are used sparingly to provide essential amino acids. Among the prosperous communities most diets provide 12 per cent of the energy as protein, about 40 per cent as fat and 48 per cent as carbohydrate. In the not well-off societies cereals in general provide most of the energy at 80 per cent with proteins and fats providing 10 per cent each. Carbohydrates provide 4 kilo calories per gram as compared to 9 kilo calories per gram of fat and 4 per gram of protein.

The energy content of common foods and the duration in minutes of activity to burn off an equivalent amount is shown in table 3.1.
### Table 3.1 Energy content of common foods and the number of minutes of activity needed to burn an equivalent amount.

<table>
<thead>
<tr>
<th>Food</th>
<th>Calorie content</th>
<th>Number of minutes of activity in the column to burn the equivalent amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (250 ml)</td>
<td>166</td>
<td>126, 32, 9, 20, 15</td>
</tr>
<tr>
<td>Milk, skim (250 ml)</td>
<td>81</td>
<td>62, 16, 4, 10, 7</td>
</tr>
<tr>
<td>Apple</td>
<td>101</td>
<td>78, 19, 5, 12, 9</td>
</tr>
<tr>
<td>Banana</td>
<td>88</td>
<td>68, 17, 4, 11, 8</td>
</tr>
<tr>
<td>Orange</td>
<td>68</td>
<td>52, 13, 4, 8, 6</td>
</tr>
<tr>
<td>Bread and butter (1 slice)</td>
<td>78</td>
<td>60, 15, 4, 10, 7</td>
</tr>
<tr>
<td>Boiled egg</td>
<td>77</td>
<td>59, 15, 4, 9, 7</td>
</tr>
<tr>
<td>Beans, 1 cup</td>
<td>27</td>
<td>21, 5, 1, 3, 2</td>
</tr>
<tr>
<td>Carrot, raw</td>
<td>42</td>
<td>32, 8, 2, 5, 4</td>
</tr>
<tr>
<td>Lettuce, 3 large leaves</td>
<td>30</td>
<td>23, 6, 2, 4, 3</td>
</tr>
<tr>
<td>Peas, 1 cup</td>
<td>55</td>
<td>43, 11, 3, 7, 5</td>
</tr>
<tr>
<td>Spinach, 1 cup</td>
<td>20</td>
<td>15, 4, 1, 2, 2</td>
</tr>
<tr>
<td>Potato, boiled</td>
<td>100</td>
<td>77, 19, 5, 12, 9</td>
</tr>
</tbody>
</table>

### Table 3.2 Energy expenditure during different activities for a 70 kg person

<table>
<thead>
<tr>
<th>Form of activity</th>
<th>Energy expended / kcal per hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lying still, awake</td>
<td>77</td>
</tr>
<tr>
<td>Sitting at rest</td>
<td>100</td>
</tr>
<tr>
<td>Typing rapidly</td>
<td>140</td>
</tr>
<tr>
<td>Dressing or undressing</td>
<td>150</td>
</tr>
<tr>
<td>Walking on level at 4.8 km per hour</td>
<td>200</td>
</tr>
<tr>
<td>Cycling on level at 9 km per hour</td>
<td>804</td>
</tr>
<tr>
<td>Walking up 8% gradient at 4.8 km per hour</td>
<td>357</td>
</tr>
<tr>
<td>Sawing wood</td>
<td>480</td>
</tr>
<tr>
<td>Jogging at 9 km per hour</td>
<td>570</td>
</tr>
<tr>
<td>Rowing at 20 strokes per minute</td>
<td>828</td>
</tr>
</tbody>
</table>
Biological significance of carbohydrates

The energy stores of most animals and plants are both carbohydrate and lipid in nature. Carbohydrates are generally available as an immediate energy source, whereas lipids act as long term energy resource and tend to be utilised at a slower rate. Glucose, the free sugar circulating in the blood of all higher animals is the main energy currency. It is essential to cell function, and proper regulation of glucose metabolism is of paramount importance for survival.

Regulation of energy metabolism involves several factors including relationships between the brain, liver, muscle, pancreas, and energy stores such as fat in adipose tissue and glycogen in muscle and liver. These relationships change with the body’s activities including feeding, fasting and starvation, as well as brief exercise and prolonged period of exercise. Relationships both within and between these organs change during these activities. This is depicted in Figure 3.3

Figure 3.3 Relationships between utilization and storage of energy from food.

The overall direction of energy, towards storage or expenditure through oxidation is controlled mainly by two hormones, glucagon and insulin, both of which are secreted into the blood stream by the pancreas in response to fluctuations in blood glucose levels. Because of the large mass of muscle and fat tissue in the body, the ability of insulin to control the uptake and metabolism of glucose in these cells plays a major part in regulating the blood glucose concentration. On the other hand glucose is the main regulator of insulin secretion. Some amino acids (e.g. arginine) have a minor effect in provoking insulin secretion. Glucagon secretion is inhibited by glucose and insulin, and is stimulated by amino acids. Other hormones that play a part in regulating energy metabolism include epinephrine, nor-epinephrine and thyroid hormone. These hormones also act on various target organs to influence energy metabolism.
The brain stores very little energy, and relies almost exclusively on a constant supply of glucose from the blood stream. Hence the supply and maintenance of the brain’s source of energy is important. The liver, on the other hand, tends not to consume much glucose for its own purpose. Instead it burns fat. Skeletal muscle uses a variety of fuels including glycogen for its work.

Carbohydrate containing foods such as starch are digested to glucose, which is then absorbed into the blood. Once a glucose molecule has passed from the blood stream into a cell it gets metabolised in a controlled way through several biochemical steps controlled by enzymes, some of which need co-factors derived from vitamins.

To conserve the energy released from burning glucose as ATP three metabolic pathways are involved. First glucose is oxidised through the pathway known as glycolysis. As an end product two molecules of pyruvate are produced, which are then fed into the citric acid cycle (also called tricarboxylic acid or Krebs oxaloacetate cycle) where they are completely oxidized to carbon dioxide and water. The energy is released in the form of ATP, such that 1 molecule of glucose gives rise to 31 of ATP. Glycolysis occurs inside the cytosol, following which pyruvate passes into the mitochondria for further oxidation. (See Fig. 3.4).

![Figure 3.4 Oxidation of carbohydrate to produce energy](image)

The energy produced by metabolic breakdown of different fuels may be released only as heat. But more often, the energy released is captured by the concomitant formation of a high energy bond, e.g. ATP. Glycolysis as well as the tricarboxylic acid cycle contain steps where these types of high energy bonds are formed. Most ATP formation occurs in the mitochondria coupled to the operation of the respiratory chain where oxygen is combined to carbon and hydrogen atoms resulting in the formation of carbon dioxide and water. Hence the term “oxidative phosphorylation”. The ATP
produced in the mitochondria gets transported out to the cytoplasm and elsewhere as energy source for doing metabolic work like synthesis of proteins, lipids, nucleic acids, and so on.

![Chemical structure of ATP (Adenosine triphosphate)](image)

**Figure 3.5 Chemical structure of ATP (Adenosine triphosphate)**

**Energy stores.**

If a body cell needs energy and glucose is available, then the glucose will be oxidised by the glycolytic pathway and the citric acid cycle with the formation of ATP. If, however, there is surplus glucose then the capacity of the citric acid cycle in the mitochondria gets overwhelmed. Glycolysis is inhibited and the excess glucose is channelled towards formation of glycogen. The process is called glucogenesis.

The liver and muscle are important storage sites of glycogen. The average adult has 70 g of glycogen in the liver and 200 g in the muscle. The liver glycogen reserves are sufficient at the most for an overnight fast. So during strenuous work the body must switch to fat reserves for energy. Thus in between meals the liver glycogen stores maintain blood glucose levels.

As we have seen food energy which is not immediately used up gets stored for future use, and that there are two types of such stored energy – short term stores viz. glycogen, and long term storage viz. adipose tissue. The deposition of nutrients as energy stores requires the expenditure of energy for the synthesis of glycogen and triglycerides. The energy cost of depositing dietary fat as adipose tissue is relatively low being equal to 3 per cent of the total amount of energy. The cost of depositing dietary carbohydrate as glycogen is about 7 per cent of the energy contained in the carbohydrate. The energy cost of converting dietary carbohydrate to triglycerides is relatively high. It is equivalent to about 23 per cent of the energy in the carbohydrate. Thus excess consumption of fat in the diet is more efficient in laying down adipose tissue in the body.
Pregnancy and lactation bring about major changes in energy metabolism. Food consumed by the pregnant woman is used directly for the synthesis of new maternal and foetal tissues, is burnt to provide energy for the increase in biosynthetic activity and for the deposition of fat stores to be utilised later during lactation. The total weight gain in healthy woman on an adequate diet is about 10 to 12 kg. The infant represents about a third of this weight (3.3 kg). The increase in maternal fat stores is also in the region of 3 to 3.5 kg, representing 30 000 kcal of energy.

During lactation the energy requirement is increased by about 500 kcal/day. The energy content of the typical milk output of 800 ml/day is about 575 – 600 kcal/day. The extra fat deposited during pregnancy is mobilized together with dietary energy to provide the energy contained in breast milk and to support the energy cost of the metabolic work of synthesis and secretion of milk.

Fig. 3.6 summarises how glucose is dealt with by the body’s metabolic pathways.

Figure 3.6  Fate of glucose
Proteins.

Proteins constitute the soft tissue of the lean body as well as the hundreds of enzymes involved in biochemical activity. These proteins are in a state of flux, being continually broken down and re-synthesized at various rates. In the process proteins are converted into their constituent amino acids, some of which are de-aminated and used up in energy production by entering the citric acid cycle. The amino groups are concentrated in urea and excreted in the urine. This on-going process of break down and re-synthesis is called protein turnover. Small quantities of protein and amino acids are also lost in the urine and faeces. Faecal proteins and amino acids arise partly from the protein of the digestive juices and partly from the cells sloughed off from the gut mucosa. Other nitrogenous compounds such as creatinine and uric acid are also excreted in the urine. The amount of nitrogen lost from the body as a result of the breakdown of body’s own proteins and amino acids is called the obligatory nitrogen loss. Dietary protein is needed to replace these losses. The amount of protein required to replace the obligatory losses is called the protein required for maintenance. Both adults and children have maintenance requirements for protein. Children and pregnant women have the additional requirement of extra protein for growth, and in the case of lactating women for the protein in the milk. The current recommendation (FAO/WHO – 1985) is 52.5 g for a 70kg man and 41g for a 55 kg woman. For children the recommendation starts at 1.85 g/kg body weight in young infants and falls to 1 g/kg body weight by the age of five years. The maintenance need is a direct reflection of the rates of metabolic pathways that consume amino acids. The metabolic need is a function of the genotype as well as the developmental, nutritional and physiological state of the individual. The maintenance needs can be divided into those directly associated with protein deposition which is a critical issue in paediatric nutrition, and those associated with the maintenance of body protein balance, which is more important in adult nutrition. The current recommended dietary allowances (RDA) of intake of high quality protein lies between 96 and 125 mg of nitrogen/kg (equivalent to 600 to 800g protein/kg). RDAs are primarily designed for populations rather than individuals since individual needs vary. They represent ‘safe level’, arrived at by adding 2 standard deviations to the mean. (See Fig. 3.7)
During pregnancy protein is needed for the growth of the foetus, the placenta, the uterus, and the mother’s breasts as well as other tissues. There is also increase in the mother’s red cell mass and plasma volume, both of which require protein. The foetus’ demand for protein is slight to begin with, but during the last month of pregnancy it lays down almost half of its total protein. In the process of accumulating this store and building a reserve for the period after delivery, the mother on an adequate diet retains between 2 to 3g of nitrogen daily during pregnancy (1g nitrogen = 6.25 g of average protein). By the end of pregnancy the mother and the foetus will have acquired approximately 500 g of nitrogen.
Proteins are polymers of amino acids. Eight amino acids are essential. They are required but cannot be produced by the body. These amino acids are: isoleucine, leucine, lysine, methionine (which can be partly replaced by cystine), phenylalanine (which can be partly replaced by tyrosine), threonine, tryptophan, and valine. In some situations histidine appears to be essential. These amino acids are not all required in the same amount each day. For example, leucine is required most and tryptophan least. Because amino acids are not stored in the body they will be most efficiently used when a complete assortment is supplied at about the same time. Tissue synthesis requires the presence of all essential amino acids. If any one of them is present in sub-optimal amounts the process of tissue deposition will be proportionately compromised. (See Fig 3.8)
Figure 3.8 Synthesis of tissue proteins

The image on the left shows tissue synthesis with a full complement of the essential amino acids. That on the left illustrates reduced rate of synthesis because of lack of one of the essential amino acids (lysine). This observation is the basis for the term ‘limiting amino acids’.

Foods vary in the amount of proteins they contain per 100g. They also vary in the nutritional value, or quality, of their proteins because of differences in the pattern of essential amino acids they contain. (Table 3.4). Overall proportions of amino acids in a food of vegetable origin differ from those needed by humans. For example, wheat and rice proteins are comparatively low in lysine, and lentils are low in tryptophan and methionine. These proteins are said to have low biological values because protein quality is determined by its ability to supply all the essential amino acids in the amounts needed. Mixtures of vegetable proteins can complement each other and result in greatly enhanced values.

Most animal proteins have high biological value since they can be utilized by humans for tissue repair and growth. Another advantage that foods of animal origin have is the presence of nutrients like vitamin B12, iron and retinol.
Table 3.4 Essential amino acid patterns of some common foods. (mg. of amino acid per 1g of protein). Limiting amino acids are highlighted.

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Breast milk</th>
<th>Cow's milk</th>
<th>Meat</th>
<th>Egg</th>
<th>Wheat flour</th>
<th>Maize flour</th>
<th>Soy bean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histidine</td>
<td>24</td>
<td>27</td>
<td>41</td>
<td>25</td>
<td>25</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>47</td>
<td>53</td>
<td>48</td>
<td>55</td>
<td>39</td>
<td>39</td>
<td>51</td>
</tr>
<tr>
<td>Leucine</td>
<td>90</td>
<td>97</td>
<td>86</td>
<td>88</td>
<td>75</td>
<td>128</td>
<td>82</td>
</tr>
<tr>
<td>Lysine</td>
<td>60</td>
<td>81</td>
<td>95</td>
<td>72</td>
<td>25</td>
<td>28</td>
<td>68</td>
</tr>
<tr>
<td>Methionine + Cystine</td>
<td>36</td>
<td>35</td>
<td>41</td>
<td>59</td>
<td>46</td>
<td>41</td>
<td>33</td>
</tr>
<tr>
<td>Phenylalanine + tyrosine</td>
<td>75</td>
<td>84</td>
<td>76</td>
<td>93</td>
<td>84</td>
<td>104</td>
<td>95</td>
</tr>
<tr>
<td>Threonine</td>
<td>39</td>
<td>41</td>
<td>49</td>
<td>46</td>
<td>30</td>
<td>40</td>
<td>41</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>13</td>
<td>13</td>
<td>11</td>
<td>15</td>
<td>11</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Valine</td>
<td>51</td>
<td>64</td>
<td>50</td>
<td>68</td>
<td>44</td>
<td>52</td>
<td>52</td>
</tr>
</tbody>
</table>

Proteins of vegetable origin usually have lower nutritive values because they have suboptimal amounts of one or more essential amino acids. However, when vegetable proteins are combined in the diet the overall amino acid combination is improved. This is the basis for using food mixtures (e.g. double mix and quadric-mix) as weaning foods for young children.

**Amino acids.** Amino acids are so called because of the presence of a nitrogen atom. (See Fig. 3.9)

![General formula of an amino acid](image)

**Figure 3.9** Chemical structure of amino acid
The average ratio of protein: nitrogen by weight is 6.25 for the typical protein in the diet. This number is used as a conversion factor for expressing the amount of protein in the diet and for the protein equivalent excreted in the urine or faeces in the form of nitrogenous waste product. Using the above conversion factor 16g of nitrogen is equivalent to 100g of protein.

The weight of protein per unit of energy in the food is called the **protein density**. Beans and peas and other legumes which are good sources of protein have protein densities similar to that of eggs. Cereals including rice, wheat and maize are moderately good sources of protein. The protein density of rice is a bit lower than that of wheat products like bread and spaghetti, and also that of maize. Plantains, cassava, taro and sweet potato which are major staples in some parts of the tropics have protein density well below that of maize, wheat or rice. As such they are poor sources of protein.

Besides the amount of protein in a food its quality is of major importance. Protein quality is about the ability of a particular protein to provide a balanced pattern of essential amino acids. A high quality protein contains all essential amino acids in appreciable amounts. A low quality protein is deficient or lacking in or more of these amino acids. Although beans and eggs are similar with regard to protein density, the quality of egg protein is considerably better than that of protein in beans.

**Protein metabolism.**

Dietary protein is digested in the gastro-intestinal tract to release its 20 constituent amino acids. Unique pathways are followed by the catabolism of each of the amino acids. Depending upon the body’s requirement some amino acids may be utilised immediately for body tissue synthesis. Those that are surplus to immediate requirement are used for energy production after deamination.

![Diagram of protein metabolism](image)

Amino acids which are not immediately utilised for tissue synthesis are broken down to yield carbon skeletons that can enter the citric acid cycle for energy production. Those amino acids that
enter through the pyruvate gateway are referred to as glucogenic since they can be withdrawn and used of gluconeogenesis. Others are catabolized to yield acetyl-coA, and can be used for making ketone bodies. These amino acids are referred to as ketogenic. These terms viz. glucogenic and ketogenic indicate metabolic pathways that are open to amino acids.

![Amino acids in energy metabolism](image)

Figure 3.10 Amino acids in energy metabolism

Amino acid requirement vary with age and with the health status of the individual. Some amino acids have special relevance to the age of the individual. For example, all current amino acid RDAs for infants use the amino acid pattern of human milk as the standard, and not that of egg protein as was the custom in the past. (See table 3.5.)

Table 3.5 Recommended levels of protein and essential amino acid intake for infants and children

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Protein intake (g/kg/day)</th>
<th>Lysine</th>
<th>Phenylalanine + tyrosine</th>
<th>Methionine + cysteine</th>
<th>Histidine</th>
<th>Valine</th>
<th>Isoleucine</th>
<th>Leucine</th>
<th>Threonine</th>
<th>Tryptophan</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 0.1</td>
<td>2.69</td>
<td>191</td>
<td>223</td>
<td>97</td>
<td>62</td>
<td>137</td>
<td>142</td>
<td>280</td>
<td>118</td>
<td>46</td>
</tr>
<tr>
<td>0.1 – 0.25</td>
<td>1.91</td>
<td>136</td>
<td>159</td>
<td>69</td>
<td>44</td>
<td>97</td>
<td>101</td>
<td>199</td>
<td>64</td>
<td>33</td>
</tr>
<tr>
<td>0.5 – 1</td>
<td>1.32</td>
<td>94</td>
<td>110</td>
<td>47</td>
<td>31</td>
<td>67</td>
<td>70</td>
<td>137</td>
<td>58</td>
<td>22</td>
</tr>
<tr>
<td>1 – 2</td>
<td>1.12</td>
<td>72</td>
<td>82</td>
<td>34</td>
<td>24</td>
<td>46</td>
<td>46</td>
<td>95</td>
<td>44</td>
<td>26</td>
</tr>
<tr>
<td>2 – 4</td>
<td>1.05</td>
<td>61</td>
<td>66</td>
<td>26</td>
<td>21</td>
<td>36</td>
<td>29</td>
<td>69</td>
<td>36</td>
<td>23</td>
</tr>
<tr>
<td>5 – 10</td>
<td>0.91</td>
<td>52</td>
<td>57</td>
<td>23</td>
<td>18</td>
<td>32</td>
<td>26</td>
<td>61</td>
<td>31</td>
<td>10</td>
</tr>
</tbody>
</table>
A convenient way of viewing amino acid nutrition in the past was to consider two categories viz. essential and non-essential. This distinction becomes blurred when we come to consider amino acid metabolism. Amino acids that are not essential in the adult may have to be provided in the diet of a child. In the normal adult there are metabolic pathways that lead to the formation of some amino acids. Under normal circumstances the flow through the pathway is adequate to satisfy the body’s demands. But when metabolism is altered or the need for an amino acid increases for either physiological or pathological reasons there may be insufficient synthesis of the amino acid, which then becomes “essential”. For example, in chronic renal disease the need for dietary histidine becomes apparent because of impaired renal synthesis of histidine. A convenient way of viewing amino acid nutrition is to think of three groups; essential, non-essential and conditionally essential. This third group is characterised by three features:

1. Their synthesis uses other amino acids as precursors. This is an important distinction from the non-essential amino acids. For some conditionally essential amino acids the precursor is an essential amino acid e.g. phenylalanine is required for the synthesis of tyrosine. But for others the precursor is a non-essential amino acid e.g. glutamate is needed for the synthesis of arginine and praline. For others like cysteine both essential (e.g. methionine as sulphur donor) and non-essential (e.g. serine as carbon donor) amino acids are required. This demonstrates that at the metabolic level the ability of the host to synthesize a conditional essential amino acid may be constrained by the availability of a suitable precursor amino acid.

2. Their synthesis may be confined to specific organs. In recent years the role of the intestine in the synthesis of proline and arginine has come to be understood. Moreover, a dietary source is crucial for both these amino acids. Therefore, alterations in intestinal metabolism in disease states or in dietary intake can influence the host’s ability to synthesise these amino acids. This has a bearing on parenteral nutrition.

3. In certain situations the maximum rate at which synthesis of conditionally essential amino acids can proceed may be limited. For example in very low birth weight infants the ability to synthesize cysteine and proline is not fully developed. In the case of the adult, some disorders impose demand on the metabolism of conditionally essential amino acids which can outstrip the host’s ability to synthesise them. This has been described for proline nutrition in severely burnt patients and for cysteine in chronic infections.

**Synthesis of proteins**

Tissue proteins are species specific, and within each species, unique to the individual. This is the reason why ingested proteins must be digested to their constituent amino acids, which are then reassembled with genetic imprint of the individual.

Synthesis of proteins in the body occurs within cells on structures called ribosome. Some ribosomes float free in the cytoplasm, and some are bound to the endoplasmic reticulum which is a network of interconnected tubules in the cytoplasm (See Fig. 3.12).
When amino acids get assembled into some newly formed protein, it moves along in the endoplasmic reticulum and is finally discharged into a secretory vesicle. The secretory vesicle then delivers its cargo into the cell, or in some instances outside the cell into the extracellular fluid.

The cell nucleus contains its genetic material which determines the properties and functions of the cell. According to the genetic code carried on the DNA molecule in the cell, messenger RNA (mRNA) is released into the cytoplasm. Unlike the DNA which is a double helix mRNA occurs as a long linear strand and contains the information needed for the synthesis of a specified protein in the form of a sequence of bases. The bases are guanine (G), cytosine (C), adenine (A), and thymine (T). Each sequence is in the form of triplets of bases, a triplet being a code for a specific amino acid. For example, the triplet UUU codes phenylalanine, CAU codes histidine; GAG encodes glutamate, AAA codes lysine, and so on. Besides these codes mRNA also contains information that influences the rate of translation. Messenger RNA binds to the surface of the ribosome which serves as a biochemical brace aligning the mRNA and amino acids to form the required polypeptide chains. The codes on the mRNA are recognised by another RNA molecule called transfer RNA (tRNA). Its job is to selectively bind to the appropriate amino acids and make them available at the right point during protein synthesis. There are at least 20 different types of tRNA and activating enzymes that correspond to the 20 amino acids commonly found in protein. Unlike mRNA which is a linear strand tRNA can spontaneously fold and twist to form an oblong structure. It functions as biochemical pliers holding the required amino acid for adding to the growing polypeptide chain at the ribosome / mRNA complex. (See Figs. 3.12, 3.13 and 3.14).
Figure 3.12 The DNA molecule

Figure 3.13 Stepwise schematic representation of protein synthesis
Being three dimensional the resulting protein has a characteristic shape that suits it to its unique biological task. A protein in the wrong shape can be a problem, sometimes causing illness and disease. Using high-energy physics techniques, structural biologists have identified the shapes and sizes of various proteins in our body. The shapes of haemoglobin and insulin are shown in Fig. 3.15 as examples.
All proteins fall into one of two classes – fibrous and globular. Fibrous proteins are generally used as structural material in the body. They are an important part of skin, hair and finger nails as well as collagen. They tend to have repeating segments of similar amino acids. Collagen, the most abundant protein in the body, is formed from a chain of about 1000 amino acids. The main ones are glycine, praline, and hydroxyproline.

Globular proteins are of a fixed chain length and have a strict order of amino acids. Thus all the molecules of a particular globular protein are identical. Each globular protein has the same specific job to do in the body, be it breakdown of food, transferring information in the body, or fighting bacteria. Only if it has the right sequence of amino acids will it have the correct activity. Furthermore, the sequence of amino acids in any particular group of globular proteins is specific to that protein, and the sequence varies greatly between one type of globular protein and another. Globular proteins have a precise overall shape arrived at by being folded into that shape. Such a precise three-dimensional shape is necessary for the activity of the protein. Only this shape will do. Loss of shape is called denaturation, and is usually accompanied by loss of activity of the protein.

**Biological Significance of proteins.**

Proteins are the ‘doers’ of the cell. They are huge in number and variety as well as different in structure and function. They serve as both the structural building blocks and the functional machinery of the cell. Their various functions may be listed as follows:

- Enzymes are the largest functional group of proteins.
- Mechanical support in the form of cytoskeleton and extracellular matrix.
- Communication in the form of cytokines (for signals between cells) and receptors (for recognizing signals) and transducers (for interpreting and reacting to signals).
- Adhesion between cells and between cell and its extracellular matrix.
- Movement in the form of motor proteins.
- Defense in the form of antibodies.
- Transport both within the cell and to and from the cell.
- Storage e.g. ferritin which binds iron and stores it in the liver.
Role of protein in body’s defense mechanisms.

Both the cellular and humoral defense mechanisms require adequate protein intake. This would be discussed further under protein-energy malnutrition. Here the two important contributions to body’s defenses are mentioned:

1. An important part of barrier function to microbial invasion in the lungs and gastro-intestinal system is the continual secretion of mucous glycoproteins. The amino acid threonine forms an important part of the glycoprotein complex.
2. Amino acids are needed to support the synthesis of the cellular proteins of the immune system and to support the hepatic acute-phase protein response.
3. Glutathione helps to mop up free radicals. Levels of glutathione are depleted in the liver and intestine, its two major sites of production, in experimental animals fed protein restricted diet.

A number of amino acids perform key functions in the body’s physiology. Glutamine, an amino acid which is largely concentrated in the skeletal muscle, plays a specific role in maintaining the function of rapidly proliferating tissues like lymphocytes and the cells of the intestinal mucosa. Under conditions of infection and trauma, muscle concentration of glutamine fall. Taurine is an effective scavenger of peroxides.

A considerable amount of amino acid metabolism occurs in the tissues of the splanchnic bed and in the intestinal mucosa in particular. Intestinal amino acid utilization may account for as much as 50% of whole body turnover of amino acid, and the degree to which individual amino acids are utilized may vary among the amino acids. Among the essential amino acids the utilization of threonine is particularly high, and virtually all the dietary glutamate and aspartate is utilized by the intestine.

Amino acids also play a critical role in intestinal energy generation. At least 50% of intestinal carbon dioxide production arises from metabolism of glutamate and aspartate. Glutamine is considered to be the preferred fuel for the gut. After trauma, surgery or sepsis the intestinal tract increases its rate of glutamine consumption. Several studies have shown that glutamine supplementation improves the structural integrity and growth of the intestine during catabolic conditions associated with gastro intestinal diseases, sepsis, and diarrhoea as well as after total parenteral nutrition.
Figure 3.16 summarizes the fate of amino acids in the body.
Fats and oils

These comprise a large group of water insoluble substances predominantly made up of glyceryl esters of fatty acids (triglycerides). Fats are distinguished from oil only by their different melting points. At room temperature fats are solid and oils liquid. The term ‘fat’ is used to refer to the whole group, and is synonymous with lipids. It includes not only visible fats (like butter and margarine), cooking fats and oils but also ‘invisble fats’ which occur in foods like cheese, biscuits, nuts and other animal and vegetable foods. They are a more concentrated form of energy than carbohydrates, and are the form in which energy reserves of animals and some plants as well as seeds are stored.

Dietary fat serves five important functions:

1. A source of energy.
2. For cell structure and membrane functions.
3. As a source of essential fatty acids.
4. As a vehicle for fat soluble vitamins.
5. For control of blood lipid levels.

Fats also contribute to the palatability of the diet and have a useful role in cooking and food processing.

In the body fat occurs in two forms:

**Storage fat** is mainly in the form of triglycerides and occurs in specific depots. As the name implies it serves as energy reserve. Each triglyceride is a combination of three fatty acids with a unit of glycerol, and the differences between one fat or oil and another are largely the result of the different fatty acids. Fatty acids present in the triglycerides are usually related to the diet.

**Structural fat.** It consists mainly of phospholipids and cholesterol. Structural fat constitutes an important part of the soft tissue of the body and occurs in high concentration in the brain. The fatty acid components of the phospholipids are of crucial importance in their function as constituents of cell membranes. The fatty acids of phosphoglycerides generally exhibit tissue and species specificity. Their composition changes only in extreme situations. The chemical formulae and structure of glycerol, triglycerides and phospholipids are shown in Fig.3.17.

**Dietary fat** consists primarily (98%) of triacylglycerol, composed of one glycerol molecule combined with (esterified) three fatty acid molecules, and remaining 2% or so made up of phospholipids and sterols. Except for the brain and red blood cells all other tissues of the body use fatty acids as a ready source of energy. The brain can use ketones derived from fatty acids as energy source.

Fatty acids are chains of hydrocarbons that contain a methyl (-CH3) and a carboxyl (-COOH) end. Fatty acids vary by the number of carbon atoms in the chain and by the presence and position of double bonds. The position of the first double bond from the methyl end of the chain is used for identification of the fatty acid. As described later the position of the first double bond is given a prefix “n” or “ω”.
The major saturated fatty acids in food derived from animal source are palmitic (C16:0), and stearic acids (C18:0). The most prevalent mono-unsaturated fatty acid is oleic acid (C18:1 \( \omega-9 \)). It is derived from plants or synthesized in the body. Linoleic acid (C18:2 \( \omega-6 \)) is the major poly unsaturated fatty acid derived from plants; \( \alpha \)-linolenic acid (C18:3 \( \omega-3 \)) is also found in plant oils and its derivatives come from animals (fish are an important source) that ingest them. Human milk contains substantial quantities of C18 precursors of the \( \omega-3 \) and \( \omega-6 \) families as well as their precursors.

The basic structure of a triglyceride is the same irrespective of whether the fat comes from animals e.g. milk and butter, or is in meat, or from plants, as cooking oil, olive oil or margarine. The number of carbon atoms in the fatty acids is always an even number. This is because the building blocks from which fatty acids are made contain two carbons. So, however many building blocks are added together the chain always contains an even number of carbons.

A fat or oil is made up of a mixture of different triglyceride molecules, each derived from different combinations of three fatty acids. Although some of the triglycerides will be made from three identical fatty acids, the majority of triglyceride molecules are derived from two or three different fatty acids. The way the fatty acids are combined to make the triglycerides is not random. The proportion of each triglyceride molecule is controlled by the organism to give the fat the required proportion.

Fatty acids fall into two main groups – saturated and unsaturated. In saturated fatty acids all carbon atoms are joined by single bonds and the remaining valency bonds are occupied by hydrogen except for the carboxyl group. In other words, they have as many hydrogen atoms as the carbon atoms can hold. When hydrogen atoms are missing the carbon atoms form a double bond. In mono-unsaturated fatty acids two adjoining carbon atoms are joined by a double bond. In poly-unsaturated fatty acids there is more than one double bond. These react gradually with the oxygen in the air and the fat goes rancid.
All fats contain a mixture of saturated, mono-unsaturated and poly-unsaturated fatty acids, but in widely varying proportions depending on the source. The presence of large amounts of unsaturated fatty acids affects the physical as well as the chemical properties of a fat making it liquid at room temperature. Figure 3.18 gives the chemical formulae of saturated and unsaturated fatty acids, and Fig.3.19 depicts the typical forms of triglycerides in vegetable animal and fish sources.

Figure 3.18 Saturated and unsaturated fatty acids

Figure 3.19 Typical triglycerides of vegetable animal and fish origins.
Fatty acids are conventionally classified according to their chain length as short chain (<8 carbon atoms), medium (8 to 11 carbon atoms), intermediate (12 to 15 carbon atoms) and long chain (≥16 carbon atoms). Abbreviations are used to describe fatty acids which indicate the number of carbon atoms, and double bonds as well as the position of the terminal double bond. The carbon atoms are labelled from the carboxylic acid end. Either the carboxylic carbon is labelled C1, followed by C2, C3, C4, and so on; or the first carbon atom after carboxyl group is labelled Cα, and so on through the Greek alphabet. The last carbon atom in the chain, which is the CH3 end, is referred to as the “omega” (Cω) carbon. The carbon atom chain length is the major determinant of melting point, energy content per gram, degree of solubility in water and other solvents, and hence the efficacy of absorption in the intestinal lumen, as well as metabolic properties such as effects on lipoprotein metabolism, oxidative breakdown, and tissue fat deposition. Fatty acid properties are also modulated by the number, type and position of double bonds ranging from none (saturated fatty acids) to one (mono-unsaturated) or more (poly-unsaturated).

Infants and young children need relatively large amounts of polyunsaturated fatty acids which are indispensable components of lipids in the cell membranes of tissues. They modulate membrane functions like membrane fluidity, activity of membrane bound enzymes, and receptors, metabolic exchange, and signal transduction. The availability of polyunsaturated lipids has been shown to affect the functional development of the central nervous system during the phase of rapid growth in infancy.

**Essential fatty acids.**

**Nomenclature.** Fatty acid formulae have been abbreviated in the form x: y, n-m, where x = number of carbon atoms in the molecule, y = number of double bonds, and m = position of the first double bond numbered from the methyl end. Thus palmitic acid is 16:0 (16 carbon atoms, no double bond). In other words a saturated fatty acid. Linoleic acid is 18:2, n-6 (18 carbon atoms, two double bonds, the first double bond occurring at carbon atom 6 from the methyl end). Arachidonic acid is a polyunsaturated fatty acid containing a 20 carbon atom chain with 4 double bonds, the first of which occurs at the position of the sixth carbon from the methyl end. It is C20:4, n-6. The terminal methyl end is also called the omega end. This part of the fatty acid molecule is minimally changed during metabolism because fatty acids are metabolised by co-enzyme A at the carboxyl end. Biochemical reactions like chain elongation or shortening, or the introduction of new double bonds occur through the carboxyl end of the molecule. The omega end remains intact unless the fatty acid is completely oxidised to carbon dioxide. Humans can elongate fatty acids to extend chain lengths, and in some circumstances can desaturate the chain to make double bonds. However, we cannot introduce double bonds in the n-6 and n-3 positions (six and three carbon atoms away from the omega end). Hence n-6 poly-unsaturated fatty acid (n-6 PUFA) which is linoleic acid, and n-3 PUFA which is α-linoleic acid are essential nutrients that must be provided from external resources.

Many fatty acids that make up the lipid components of biological membranes are unsaturated. Unsaturated fatty acids have very different physical properties from saturated fatty acids, and crucially affect the properties of the membrane in which they occur.

Linoleic (18:2, n-6) and α-linoleic acid (18:3, n-3) acids are required for the normal growth and function of all tissues. Longer chain fatty acids containing several double bonds are derived from
linoleic and α-linoleic acids are referred to as long chain fatty acids. An example is arachidonic acid (20:4, n-6). Some long chain poly unsaturated fatty acids (PUFA) are also precursors of bioactive lipid mediators including prostaglandins, thromboxanes, leukotrienes, and several others. Several PUFA are indispensable components of plasma membranes, and occur in large amounts in membrane rich tissues such as the brain and retina. PUFA comprise of a wide range of 18, 20 and 22 carbon chain lengths with two to six double bonds.

The effect of omega-3 fatty acid consumption has been investigated both by epidemiological studies as well in cell culture and in animal studies. Dietary omega-3 fatty acids have a cardio protective function. They seem to stabilize the myocardium electrically resulting in reduced susceptibility to ventricular arrhythmia. They have potent anti-inflammatory effect and may also be anti-thrombotic and anti-atherogenic. They are being advocated as part of secondary prevention strategy in post myocardial infarction.

**Intrauterine supply of PUFA**

Intrauterine growth during the latter part of pregnancy is characterised by rapid deposition of fat, which exceeds that of any other nutrient and accounts for about 75 per cent of the energy retained in the newly formed tissues. Analysis of tissue composition from deceased infants and foetuses of different gestational ages has demonstrated a very rapid incorporation of long chain polyunsaturated fatty acids especially arachidonic acid (C20:4n-6) and docosahexaenoic acid (DHA, C22:6n-3) into structural lipids of the brain, retina and other tissues during the latter part of pregnancy. Particularly high concentrations of long chain poly unsaturated fatty acids are found in the phospholipids of membranes with high fluidity, such as synapses and retinal photoreceptors. Intrauterine supply of PUFA to the foetus depends entirely on placental transfer.

**PUFA supply through human milk**

Human milk lipids provide not only linoleic and α-linolenic acids but also considerable amounts of pre-formed long chain PUFA, the concentration of which changes with the duration of lactation.

The medians and ranges for the percentage contents of PUFA in human milk as calculated from the results of 14 European and 10 African studies on the fatty acid content of mature human milk provide base line data. The median content of linoleic acid (11% European and 12% African), α-linolenic acid (0.9% and 0.8%), arachidonic acid (0.5% and 0.6%), and DHA (0.3% for both study groups) were surprisingly similar in spite of very different diets and life styles. However, the overall ranges of reported values were wide (linoleic acid 5.7% to 17.2%; α-linolenic acid 0.1% to 1.44%; arachidonic acid 0.2% to 1.2%; DHA 0.1% to 0.9%). These variations reflect not only biological variations but also differences in methodologies used in the various studies. More recent assays using gas-liquid chromatography show that the variation of linoleic and arachidonic acids to be within a narrow range. By contrast there more than four-fold differences were found between the lowest and highest values of α-linolenic acid and DHA. Radio isotope studies in a small group of mothers show that about 30% of milk linoleic acid is directly transferred from the maternal diet. The major portion of poly unsaturated fatty acids in human milk is derived from maternal body stores. Thus the influence of maternal diet on milk composition is moderated by much larger
contribution from maternal body stores, resulting in a relatively constant milk PUFA supply to the infant.

All the functional components of dietary fats like triglycerides, cholesterol, phospholipids, and so on are fundamental to normal growth and development of infants. Each class of fatty acids is involved in specific metabolic reactions. Short chain fatty acids act as local growth factors in the colon. Medium chain and saturated long chain fatty acids are a good source of energy. Poly saturated long chain fatty acids are involved in metabolic regulation, and very long chain fatty acids are important structural components of membranes.

**Effect of PUFA on the immune system**

Recent work has shown that the production of nitric oxide and of cytokines such as interleukins-1α and β, interleukin 2, and tumor necrosis factor α are strongly modulated by n-3 fatty acids.

**Dietary sources of unsaturated fatty acids**

Unsaturated fatty acids, as we have seen are mono-unsaturated or poly-unsaturated. The mono-unsaturated fatty acids are omega 9 fatty acids, and are found mainly from plant sources like olive oil, avocados, peanuts and almonds.

The poly-unsaturated fatty acids are of two types viz. omega 3 and omega 6 fatty acids. Omega 3 fatty acids are derived from the plant kingdom e.g. α-linolenic acid found in flaxseed, soybean, walnut, and rapeseed oil; or marine derived e.g. Eicosapentanoic acid (C20:5n-3), and Docosahexanoic acid (C22:6n-3) both of which occur in fish and shell fish. Omega 3 and Omega 6 fatty acids are essential poly-unsaturated fatty acids. (See Fig.3.20). Cooking oil from corn oil and sunflower oil is rich in linoleic acid which is an omega 6 fatty acid, but humans lack the necessary enzymes to convert omega 6 to omega 3 fatty acid, which must be obtained from other dietary sources. A number of cardio-beneficial properties have been ascribed to omega 3 fatty acids as a result of clinical trials. These properties are anti-arrhythmic, anti-atherosclerotic, anti inflammatory, lowering blood triglyceride level and so on. Cardiologists recommend including two meals of fish in the weekly diet to ensure cardio vascular well being.
Dietary fat.

Dietary fats are mainly triglycerides composed of fatty acids of varying lengths which may be saturated, mono-unsaturated or polyunsaturated. In some parts of the world fat of animal origin may form a large part of the dietary fat. In recent times, however, there is a swing towards vegetable fat in preference to that of animal origin.

Dietary fat is an important nutrient in its role as a source of essential fatty acids. In addition it helps to make the food palatable, and acts as a source of fat soluble vitamins. Thus, dairy fat contains significant amounts of vitamins A and D, and so do some marine oils. Almost all vegetable oils contain vitamin E, and red palm oil has substantial quantities of carotenoids (pro-vitamin A). But fats can also contain undesirable compounds like pesticides and other agricultural or industrial chemicals used for processing the fat.

Table 3.6 below provides details of the contents of common dietary fats:
### Table 3.6 Fatty Acid Content of some Foods

<table>
<thead>
<tr>
<th>ANIMAL PRODUCTS</th>
<th>Fat (g)</th>
<th>Saturated Fatty Acids (g)</th>
<th>Unsaturated Fatty Acids (g)</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>Palmitic</td>
<td>Stearic</td>
</tr>
<tr>
<td>Meats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beef</td>
<td>25.1</td>
<td>10.4</td>
<td>6.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Mutton</td>
<td>14.8</td>
<td>5.8</td>
<td>2.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Pork</td>
<td>35.0</td>
<td>11.4</td>
<td>7.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buffalo milk</td>
<td>8.7</td>
<td>5.4</td>
<td>2.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Cow Milk</td>
<td>3.5</td>
<td>2.2</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Goat Milk</td>
<td>3.8</td>
<td>2.4</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Human Milk</td>
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<td>1.5</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Poultry and Eggs</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicken</td>
<td>15.1</td>
<td>6.0</td>
<td>3.7</td>
<td>1.4</td>
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<tr>
<td>Turkey</td>
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<td>5.9</td>
<td>4.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Hens Egg</td>
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<td>3.4</td>
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<td>0.9</td>
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<tr>
<td>Fish</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cat Fish (fillet)</td>
<td>3.6</td>
<td>0.9</td>
<td>0.6</td>
<td>0.2</td>
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<tr>
<td>Herring (whole)</td>
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<td>2.9</td>
<td>1.9</td>
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<tr>
<td>Mackerel (fillet)</td>
<td>12.6</td>
<td>3.2</td>
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<td>Red Salmon (fillet)</td>
<td>8.9</td>
<td>1.4</td>
<td>0.9</td>
<td>0.2</td>
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<tr>
<td>Tuna</td>
<td>8.0</td>
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<td>1.6</td>
<td>0.3</td>
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<table>
<thead>
<tr>
<th>PLANT PRODUCTS</th>
<th>Fat (g)</th>
<th>Saturated Fatty Acids (g)</th>
<th>Unsaturated Fatty Acids (g)</th>
<th>Other</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>Palmitic</td>
<td>Stearic</td>
</tr>
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<td>Cereals &amp; Grains</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Maize, Corn</td>
<td>4.1</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
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<tr>
<td>Oats</td>
<td>7.4</td>
<td>1.4</td>
<td>1.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Rise</td>
<td>2.3</td>
<td>0.6</td>
<td>0.5</td>
<td>trace</td>
</tr>
<tr>
<td>Wheat</td>
<td>2.7</td>
<td>0.4</td>
<td>0.4</td>
<td>trace</td>
</tr>
<tr>
<td>Nuts and Seeds</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazilnut</td>
<td>68.2</td>
<td>17.4</td>
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<td>Cashewnut</td>
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<td>31.2</td>
<td>3.0</td>
<td>1.1</td>
</tr>
<tr>
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<td>4.6</td>
<td>3.2</td>
<td>1.1</td>
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<td>1.3</td>
</tr>
<tr>
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<td>8.0</td>
<td>5.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Soybean</td>
<td>17.7</td>
<td>2.7</td>
<td>1.9</td>
<td>0.7</td>
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<tr>
<td>Walnut</td>
<td>63.4</td>
<td>6.9</td>
<td>4.5</td>
<td>1.3</td>
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</table>
Fat as a source of energy.

Of the three major nutrients carbohydrate, protein and fats, fats have the highest available energy at 9 k cal/g. The degree of utilization by normal individuals of dietary fat is greater than 90 per cent. Different populations are able to stay in a good state of health on widely different intakes of fat not only with regard to the amount but also in the type of fat consumed. However, with changing lifestyle and affluence a previously healthy diet can become unhealthy. In several industrialized countries, notably the USA, up to 50% of the adult population is currently overweight which exposes them to health hazards like diabetes, hypertension and coronary artery disease. The clustering together of these adverse conditions with obesity is now being described as the Metabolic Syndrome. It is characterized by the co-occurrence of obesity (especially central obesity) high levels of triglycerides in the blood combined with low levels of high density lipoprotein cholesterol, hyperglycemia, and hypertension. As yet no consensus exists for specific thresholds of each of these traits for establishing the diagnosis of the syndrome. Inclusion of insulin resistance or diabetes itself as diagnostic components is also controversial. The individual traits of the Metabolic Syndrome cluster together to a notably greater degree than expected by chance alone,
which lends support to the existence of a discreet disorder. Obesity is a major driving force behind the clustering of the risk factors.

Until recently adipose tissue was considered merely as a depot of stored energy. Recent work indicates that the adipocyte is an active endocrine secretory cell releasing free fatty acids and producing several cytokines and hormones, including tumor necrosis factor $\alpha$ (TNF-$\alpha$), interleukins, and several other chemical substances. These substances allow the adipocyte to have an important feedback role in regulation of appetite and energy expenditure, development of insulin resistance and to participate in the atherogenic process. The most important protein in the adipocyte is adiponectin. Several studies have pointed to an important role of adiponectin in the insulin resistance of obesity.

**Digestion of lipids.**

The digestive process acts to increase the surface area of the lipids, which being hydrophobic are insoluble and aggregate together. It also must solubilize the products of digestion for ease of absorption.

Digestion begins with the action of the lingual lipase acting inside the stomach. It converts triglycerides into free fatty acids, and mono and triglycerides. Gastric peristalsis helps to churn up the fat into small particles which aids the action of the lipase. The main part of fat digestion occurs in the small intestine under the concerted action of pancreatic lipase and bile. Lipases hydrolyze triglycerides by acting preferentially at the 1 and 3 positions. Human milk and other foods contain palmitic acid (C 16:0) predominantly at the 1 and 3 positions. Human milk and other foods contain palmitic acid (C 16:0) predominantly at the 1 and 3 positions. Thus lipolysis of human milk produces C16:0 preferentially as a mono-glyceride which is very water soluble and therefore well absorbed. By contrast saturated fatty acids in vegetable oils are more or less randomly esterified to the different positions of the molecule. Hence a greater proportion of C 16:0 is liberated as a hydrophobic free fatty acid which may combine with calcium and other cations forming insoluble soaps.

In the intestine, digestion of fat proceeds under the effect of pancreatic lipase to release glycerol and fatty acids and also split products likes monoglycerols. Lecithin and to a smaller extent cholesterol enable the effective dispersion of dietary triglycerides into a stable emulsion. This dispersion which is already begun in the esophagus and stomach and further enhanced by peristalsis is necessary for exposing lipid molecules to lipases. In the intestine the dispersion of lipids is further enhanced by the conjugated bile salts. Lipolytic enzymes adsorb sequentially to the emulsified lipid droplets and enable the cleavage of esterified fatty acids. In the normal individual pre-duodenal lipolysis can contribute 20 to 30 per cent lipid digestion, and 90 per cent or more in patients with pancreatic insufficiency, as in cystic fibrosis.

Fatty acids and monoglycerides liberated by fat digestion enter the mucosal cells of the small intestine with the help of bile salts which are required for the solubilization of lipolysis products to enable their mucosal uptake. Efficacy of absorption is greater for unsaturated than for saturated fatty acids and decreases with increasing fatty acid chain length.

Inside the enterocyte the digestion of fat may be completed through the action of the intestinal lipase. Resynthesis of triglycerides occurs utilizing the mono and di-glycerides and free fatty acids. The resynthesized fat then passes into the lymphatics (the lacteals) of the abdominal cavity and thence by way of the thoracic duct into the blood where it may be detected as chylomicrons.
Oxidation of fatty acids

Fatty acids must first be made active through a reaction with ATP before they can react with enzymes intended for their breakdown. The activated fatty acid (or acyl-CoA as it is called) is now ready for further breakdown. Several enzymes, known collectively as “fatty acid oxidase” are found in the mitochondria where fatty acids are broken down by β-oxidation resulting in formation of 2 carbon fragments. These then enter the Kreb’s oxaloacetate cycle for further breakdown into water and carbon dioxide. (See Figure 3.21)

Fatty acids with an odd number of carbon atoms are oxidized by the same method of β-oxidation until a 3-carbon residue remains. This compound is converted to one of the constituents of the Kreb’s oxaloacetate cycle and further broken down to release energy.

After digestion fat travels to peripheral tissue like muscle or adipose tissue in the form of chylomicrons. These are large triglyceride rich particles that also contain phospholipids, cholesterol, fat soluble vitamins, and other protein molecules like apoprotein A. Inside the tissues epithelium bound lipoprotein lipases liberate the fatty acids and fat soluble vitamins. Dietary fat intake modulates chylomicron clearance. Unsaturated fatty acids form larger chylomicrons which are cleared more effectively by the lipo protein lipase because it has greater affinity to unsaturated fatty acids.

Besides the chylomicrons, fat transport also involves lipo proteins of which the better known are low density and very low density (LDL and VLDL) as well as high density (HDL) lipo proteins.

![Figure 3.21 Carbohydrate, protein and fat in energy metabolism](image-url)
HDL has a strong protective effect against vascular deposition of cholesterol and the development of atherosclerosis, whereas cholesterol and VLDL have an adverse effect. (See Fig. 3.22).

**Figure 3.22 Transport of very low density lipo-proteins**

LDL cholesterol tends to get deposited on arterial walls to form atheromatous plaques when it is in high concentration in blood leading to narrowing of the arteries. HDL cholesterol is desirable as it is a means of transporting cholesterol from parts of the body where there is too much of it to the liver where it can be disposed of. Cholesterol is mostly made in the liver and is carried in the blood by the two lipo-proteins. (See Fig.3.23)
Gut Flora

The gut is the natural habitat of a large and dynamic bacterial community. In the average adult the intestines contain some 300 to 500 different species of bacteria. The number of microbial cells within the gut lumen is about 10 times larger than the number of cells in the human body. Most of the bacteria are to be found in the large intestine in concentrations of $10^{11}$ to $10^{12}$ cells/g of luminal content. Bacteria make up around 60% of faecal solids.

At the time of birth the newborn’s gut is sterile but colonization occurs rapidly. Differences exist between the gut flora of breast fed and artificially fed infants, and the initial colonization determines the final permanent flora in the adult.

Main functions of the gut flora are:

1. **Fermentation of non-digestible dietary residue and endogenous mucus.** The non-digestible carbohydrates include some starches, cellulose, hemi cellulose, pectin and gum. These get broken down by fermentation into short chain fatty acids like acetate, propionate and butyrate. Butyrate is almost completely consumed by the colonic epithelium as the main source of energy. Acetate and propionate are found in portal blood and are eventually metabolized in the liver or peripheral tissue.

   The breakdown of proteins and peptides also produces short chain fatty acids, but also generates toxic substances including ammonia, amines, phenols, thiols and indols. In the caecum and ascending colon fermentation is intense with high production of short chain fatty acids, an acidic pH, and rapid bacterial growth. In the descending colon fermentation is less intense and there is little bacterial growth. Colonic organisms also play a part in vitamin synthesis and in the absorption of calcium, magnesium, and iron.

2. **Trophic function.** An important role of short chain fatty acids is their trophic effect on the intestinal epithelium. All three fatty acids have been shown to stimulate epithelial cell proliferation and differentiation in the large and small bowels in laboratory animals. A role for short chain fatty acids in prevention of pathological states like ulcerative colitis has long been suspected.

3. **Immune function.** Continuing interactions between microbes, epithelium and gut associated lymphoid tissue occur and influence the memory mechanism of systemic immunity of the host. In this respect the interaction between the gut associated lymphoid tissue and flora early in life is crucial for appropriate development of complex mucosal and systemic immunoregulatory mechanisms.