Inadequate nutritional intakes: Causes

Aim
1. To consider environmental factors that may contribute to inadequate nutritional intakes

Inadequate intakes of specific nutrients and excessive or unbalanced intakes can both result in malnutrition, which may cause illness (morbidity) and possibly death (mortality).

Nutritional adequacy is best viewed as a spectrum, rather than having fixed boundaries (Figure 36.1).

Causes of inadequate nutrition and associated diseases

Who is at risk?
Individuals who live in countries with poor food security, or who themselves are food insecure, are at risk of undernutrition, which can manifest as specific nutrient deficiencies, hunger (chronic or seasonal) or prolonged periods of starvation/famine.

Contributory factors

Disease prevalence is affected only in part by medical practice and treatment. Many environmental factors have a much greater impact on health outcomes, as they affect all aspects of people’s lives (Table 36.1). Examples include globalisation (which affects food availability, pricing and dietary patterns), the political and legislative framework within a country, the extent to which people have access to clean water, sanitation, nutrition and health knowledge and appropriate health care, and their socio-economic status (including the overall status of women in society).

The actual impact these factors may have on the health of any given individual depends on the personal choices they make (or are able to make) and their individual genetic susceptibility. Owing to this individual level of response, the effects of undernutrition may not be seen equally within a household, community or region.

Food supplies may be inadequate in quantity as well as quality. Therefore, inadequate energy intakes may be present in addition to insufficient nutrient intake.

Figure 36.1 Spectrum of nutritional adequacy

- Deficiency diseases and general debility
- Overnutrition
- Optimum nutrition
- Undernutrition
- Ill health and nutrition-related diseases
- Normal development
- Normal development
- Normal development
- Normal development
- Normal development
**Table 36.1 Potential impact of environmental factors on health outcomes.**

<table>
<thead>
<tr>
<th>Environmental factor</th>
<th>Consequence with potential impact on nutrition and health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Globalisation of crop production, trade and food supplies</td>
<td>Changes to food availability, access, pricing and dietary patterns</td>
</tr>
<tr>
<td>Political and legislative measures</td>
<td>Policies on health, education, agriculture and land ownership, import/export policies, employment, social/welfare policies, and transport (food supplies, access to markets)</td>
</tr>
<tr>
<td>Socio-economic status of groups within population</td>
<td>Access (physical and financial) to safe food of adequate nutritional quality</td>
</tr>
<tr>
<td>Health-care provision</td>
<td>Access to appropriate health care at all life stages (e.g. immunisation, antenatal care, information on infant/child feeding practices, and early recognition of disease)</td>
</tr>
<tr>
<td>Clean water and sanitation</td>
<td>Less infectious diseases and environmental contamination; reduced nutritional needs to fight infections</td>
</tr>
<tr>
<td>Education/health and nutrition knowledge</td>
<td>Awareness of the importance of diet and health care, lifestyle habits</td>
</tr>
<tr>
<td>Status of women</td>
<td>Better food production techniques by farmers</td>
</tr>
<tr>
<td></td>
<td>Generally, women may be more likely to integrate health measures within a family; higher status allows women to be involved in decision-making</td>
</tr>
</tbody>
</table>

In some diets, nutrients may appear to be present in sufficient amounts but may be unavailable as a result of:
- **Binding** to other components of the food (e.g. phytate, dietary fibre, proteins)
- **Inactivation** by food preparation methods
- **Inhibition of absorption** by other dietary factors eaten concurrently (e.g. factors that affect intestinal pH)
- **Competition** by parasitic infestation within the gut
- **Poor utilisation** (e.g. lack of carriers for absorption or transport in the blood, due to malnutrition or a genetic defect)
- **Treatment with drugs** that prevent utilisation

**Magnitude of the problem**

It is difficult to obtain accurate information regarding the extent of undernutrition in the world today because data are either not collected routinely or are affected by sudden crises such as the outbreak of war or the occurrence of environmental disasters. The growing burden of HIV/AIDS and tuberculosis makes an important contribution to undernutrition as well; however, these effects are difficult to quantify.

Despite a theoretically adequate global food supply, the Food and Agriculture Organization (FAO) of the United Nations estimates that there are approximately 868 million undernourished people in the world. The majority live in developing countries, but about 16 million live in developed countries.

Groups at risk for inadequate intakes in developed countries include:
- Large families on low income
- Marginalised groups in society (e.g. minority ethnic groups, refugees)
- The homeless
- Individuals with addictions (e.g. to drugs, alcohol, etc.)
- Those in need of care, but who are not receiving a sufficient amount (e.g. people with disabilities)

Progress is being made internationally in reducing the number of people affected by undernutrition, but results vary from one region to another. The consequences of inadequate nutrition are discussed in Chapter 37.
Inadequate nutritional intakes: Consequences

Aim
1. To consider the consequences of inadequate intakes of macronutrients and micronutrients

Assessment
Inadequate macronutrient intake will most obviously be reflected in disturbed growth among children and body weight changes among adults. These effects can be monitored using anthropometric tools (see Chapter 33). Assessment of adolescents is often neglected due to the difficulty of relating measurements to reference standards during puberty. While undernutrition in the elderly is poorly reported, it is believed to be widespread, as this age group may become increasingly dependent for food on other members of their family or communities, and develops a greater risk of disease, which can compromise nutritional status.

Consequences of undernutrition
Undernutrition can have both short- and long-term consequences, including impaired growth rate and cognitive development, reduced work capacity, compromised ability to recover from injury or trauma, increased risk of infection and developing chronic diseases (Figure 37.1). There may also be intergenerational effects through poor pregnancy outcomes and low birth weight.

Macronutrient inadequacies
Protein–energy malnutrition, which reflects serious undernutrition, may present as marasmus, kwashiorkor or a mixed picture of the two, known as marasmic kwashiorkor (Table 37.1). The exact form of the condition depends on feeding patterns.

Micronutrient inadequacies
Deficiencies of iron, zinc, vitamin A and iodine affect the greatest numbers of people worldwide (Table 37.2). Vitamin D and several other micronutrients may also be widely deficient in populations and contribute to morbidity.

Some micronutrients may become deficient when diets lack specific food groups. These include:
- Vitamin B12, when vegan diets are consumed
- Calcium, when dairy products are excluded from the diet
- Riboflavin, when diets are low in green vegetables and dairy products

Consumption of a balanced diet that contains appropriate amounts of foods from all major food groups (see Chapter 39) increases the chance of achieving adequate nutrition. Dietary variety helps to ensure an adequate diet, but may not always be possible if food supplies are limited.

Table 37.1 Conditions associated with a lack of macronutrients.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diagnostic signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marasmus</td>
<td>Extreme wasting of fat stores and atrophy of visceral tissues; attributed to a severe lack of dietary energy Alert but minimal physical activity undertaken Normal but shrivelled skin Very susceptible to infection Oedema affecting face, limbs and abdomen, also enlarged liver Irritable, lethargic and anorexic Skin often cracked and ulcerated, hair colour changes Attributed to low protein intake, associated with excessive free radical damage to liver, with insufficient antioxidants Prognosis poor</td>
</tr>
<tr>
<td>Kwashiorkor</td>
<td></td>
</tr>
<tr>
<td>Marasmic kwashiorkor</td>
<td>Severe muscle wasting together with oedema Prognosis poor</td>
</tr>
</tbody>
</table>
Chapter 37  Inadequate nutrition: Consequences

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Numbers affected</th>
<th>Causes</th>
<th>Consequences for health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>About 2 billion people worldwide; mainly women and children</td>
<td>Low iron intake or blood loss due to parasitic and malarial infections</td>
<td>Anaemia; affects cognitive development and behaviour in children, immune function, pregnancy outcome, work capacity</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Up to 250 million children with subclinical vitamin A deficiency; up to 500 000 become blind each year. Pregnant women also affected, transmits to next generation</td>
<td>Low intake of preformed sources of vitamin A and low absorption rates of precursor carotenoids</td>
<td>In the eye: loss of night vision; Bitot's spots, damage to cornea, leading to ulceration and blindness</td>
</tr>
<tr>
<td>Iodine</td>
<td>Over 16 million children born with cretinism; up to 50 million affected with poor cognitive development</td>
<td>Low levels in soils; goitrogens interfering with utilisation from the diet Low selenium levels may exacerbate low iodine intakes</td>
<td>Poor mental development in infants born to deficient mothers</td>
</tr>
<tr>
<td>Zinc</td>
<td>Up to 2 billion people</td>
<td>Low dietary intake, high levels of absorption inhibitors</td>
<td>Increased risk of infection, reduced resistance</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Up to 1 billion people and especially those living in northern climates or who usually cover up</td>
<td>Lack of skin synthesis from sunlight (due to season/latitude, pigmentation, cultural factors or lifestyle), poor dietary intake, high levels of binding factors (e.g. phytate) in diet</td>
<td>Prematurity in infants, growth failure throughout childhood, delayed sexual maturity</td>
</tr>
</tbody>
</table>

Table 37.2  Conditions associated with micronutrient deficiencies.
Aims
1 To define overweight and obesity and consider their prevalence
2 To consider the contributory factors in energy intake and energy output that lead to overweight and obesity

Definition
Overweight and obesity can be defined as an excessive accumulation of body fat. In men, healthy body fat may be 15% of total weight, while in women, this figure may be 25%, reflecting hormonal and physiological differences.

Excessive accumulations of fat may exceed 50% of total weight, contributing to major pathological consequences. Measuring body fat is not a straightforward process, although it is possible through bioelectrical impedance, hydrostatic weighing, dual-energy X-ray absorptionmetry (DEXA) and other scientific methods (see Chapter 33 for more information). Several simple surrogate measurements are used to categorise overweight and obesity. These are:
- Body mass index
- Waist circumference
- Waist/hip ratio

Prevalence of overweight and obesity
Global prevalence has been rising steeply over the last 20 years in most countries, and there are now more overweight than undernourished people across the globe:
- Rates of overweight and obesity are increasing among children and adolescents.
- In general, obesity increases with age.
- Obesity is more prevalent in lower socioeconomic groups in Western countries, but in some parts of the world, such as India, it is seen more commonly among the more affluent groups.

Public health concerns regarding these trends relate to the parallel increase in risk of associated diseases:
- Obesity is directly responsible for some 6% of deaths in the Western world and reduces life expectancy by an average of about 9 years.
- The physical, metabolic and psychological consequences of obesity are also associated with substantial morbidity from cancer, cardiovascular disease and diabetes.
- External influences on energy intake.

Contributing factors in energy intake and output

Food availability
Both the quantity and the nature of the food available to people in many parts of the world have changed substantially in the last decades. Changes include:
- Greater choice, with more variety encouraging intake.
- Food on sale around the clock and availability of fast food.
- Improved preservation methods, so food can be always available.
- Many foods require little preparation, so can be eaten immediately.

Food quantity and quality
The rising incidence of obesity implies that energy intakes exceed expenditure (Figure 56.1).

Changes that play a part include:
- Increased consumption of convenience, ready prepared or ‘fast’ food, which has a higher energy density than typical traditional diets, resulting in ‘passive overconsumption’ of energy.
• A trend to larger portion sizes becoming the norm, which also inadvertently increases food intake.
• People eating a rising proportion of their meals away from home; hence, the impact of the food industry on food quality and quantity becomes more pertinent to obesity trends.

Snacking and ‘grazing’
There is a trend away from eating regular meals to a less structured food intake, typified by consumption of snack and convenience foods and soft drinks throughout the day, rather than eating to satiety at greater intervals. Such intakes tend to be high in fat and high-glycaemic carbohydrate, as well as being generally poor sources of slowly absorbable carbohydrate and micronutrients. The body’s appetite control mechanisms are undermined in this way.

Psychological aspects
Attitudes and beliefs have a major impact on food intake. For any one individual, food intake could be affected by:
• Their mood and mental state
• Personality
• Self-image and culturally determined body images
• Socialised attitude to food
• External factors such as peer pressure, advertising and media influences

External influences on energy output
Increased mechanisation
Technological advances result in less need to use human muscle power to carry out energy-demanding manual tasks:
• There are now fewer occupations that can be classified as heavy manual work, and even tasks that were not very physically demanding have been lightened with robots and computer-driven technology. Fewer people have physically demanding jobs in agriculture, as urbanisation proceeds rapidly.
• Transport has become increasingly concentrated on the use of the car or other transportation, as opposed to walking and use of bicycles.

Leisure activity
Secular trends suggest reduced participation in active leisure pursuits:
• The widespread availability of computers and electronic home entertainment systems reduces outdoor leisure activities.
• Physical activity has for many become an item to schedule into the day, with a trip to the gym or swimming pool, rather than an intrinsic part of existence, as it was in the past.
• Increased urbanisation and road traffic, together with safety fears, may make outdoor activity less pleasant and compound the problem.

Individual susceptibility
Not everyone exposed to the same external influences on energy intake or output will experience weight gain. There is a heritable element, although this remains difficult to quantify and separate from environmental influences within families.

Genetics
In some inherited conditions, there is a clear link with obesity. Most notable among these are Prader–Willi and Bardet–Biedl syndromes.
For the great majority of cases of obesity, however, the rapid increase in incidence within a genetically stable population indicates that external factors play the major role. This does not exclude a genetic origin to susceptibility to obesity, which becomes expressed as a result of external changes.

Ethnicity
There are observed differences in patterns of weight gain between different ethnic groups, including body fat distribution and levels of adiposity at particular BMI values.

Vulnerable periods
Research from a number of areas suggests that there are periods during the life cycle when susceptibility to obesity may be programmed (in the fetus and infant) or be increased (during periods of rapid growth, including pregnancy and lactation). The latter may be linked to changes in levels of specific hormones. Age and gender are compounding factors, with patterns of weight gain in adult life differing between men and women.

Development of overweight and obesity
Weight gain occurs when the energy intake exceeds the energy output over a period of time.
This represents a positive energy balance, such that the energy supplied to the body as food is not used and is therefore stored in adipose tissue.
A reduction in energy intake, an increase in energy output, or both, are needed to remove the stored energy, create a negative energy balance and reduce body weight.

Control of energy balance
Physiological control mechanisms exist to regulate both energy intake and output. These are discussed further in Chapter 4.
For humans in modern society, both intake and output are subject to a variety of external influences. These interact with or override the internal regulatory mechanisms, creating a challenge to the maintenance of energy balance. In addition, the relative importance of these influences varies as a result of the underlying genetic make-up of the individual, dietary complexity and environmental variables.
### Aim

1. To identify some of the major health consequences associated with obesity

There is a well-recognised relationship between the prevalence of overweight and obesity and rates of morbidity and mortality worldwide. Health risks are related to BMI in a J-shaped relationship (Figure 57.1).

At the lower end of the BMI range, usually below 18.5, risk increases due to the possibility of concurrent illness that causes loss of weight, such as cancer or complications of malnutrition. Above a BMI of 25 and especially above 30, there is a progressive increase in morbidity and mortality, associated with a range of factors. These are summarised in Table 57.1.

The metabolic effects associated with insulin abnormalities are discussed in Chapter 58.

### Obesity and cardiovascular disease

Obesity is a major risk factor for cardiovascular disease (CVD), and data consistently show a higher incidence of disease with increasing BMI. However, obesity is also a risk factor in a number of the other conditions associated with CVD, such as dyslipidaemia, type 2 diabetes mellitus (and insulin resistance) and hypertension. It is therefore very difficult to separate the attributable risk to each of these comorbidities, as in addition their relative contributions may differ between individuals.

Overall, it is estimated that in subjects exhibiting the full spectrum of these conditions, CVD mortality is increased threefold. Insulin resistance alone is responsible for about 18% of the variance in CVD risk. It is clear that the deposition of large amounts of fat within the body alters normal metabolic functions and results in a number of potentially harmful changes.

### Table 57.1 Pathological consequences of overweight and obesity.

<table>
<thead>
<tr>
<th>Type of effect</th>
<th>Examples of pathologies/consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic effects</td>
<td>Type 2 diabetes mellitus (impaired glucose tolerance, insulin resistance)</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular disease, including contributory abnormalities: hypertension, dyslipidaemia, clotting defects</td>
</tr>
<tr>
<td></td>
<td>Cancers (colon, breast, endometrium, kidney and oesophagus) – associated with upregulation of cell growth or elevated hormone levels</td>
</tr>
<tr>
<td></td>
<td>Hormonal dysfunction: menstrual abnormalities, pregnancy difficulties, anatomical changes</td>
</tr>
<tr>
<td>Mechanical effects</td>
<td>Musculoskeletal (including osteoarthritis in weight-bearing joints and back pain), resulting in disability</td>
</tr>
<tr>
<td></td>
<td>Varicose veins, oedema</td>
</tr>
<tr>
<td>Surgical</td>
<td>Anesthetic risk, poor wound healing, chest infections, thrombosis risk</td>
</tr>
<tr>
<td>complications</td>
<td>Respiratory difficulties, including sleep apnoea and breathlessness</td>
</tr>
<tr>
<td>Psychological/social effects</td>
<td>Tiredness, low self-esteem, depression, agoraphobia, isolation</td>
</tr>
<tr>
<td></td>
<td>Unemployment, discrimination</td>
</tr>
</tbody>
</table>

### Figure 57.1 Relationship between BMI and risk of morbidity and mortality
Obesity and hypertension
There are several proposed mechanisms that offer an explanation for the high correlation between obesity and hypertension. These include:
- Increase in blood volume as a result of greater salt retention. This is attributed to an antinatriuretic effect of raised insulin levels.
- Changes in hormone levels affect blood pressure regulation. For example, cortisol production by adipose tissue increases, while leptin and angiotensinogen released from adipose tissue have direct hypertensive effects.
- Higher salt intakes and low levels of physical fitness may also contribute.

Obesity and cancer
Prevention of overweight is considered to be one of the strategies to prevent cancer. There is, however, a lack of clear evidence to support mechanisms by which excess weight may cause cancer.

It is proposed that in obesity:
- Receptors for insulin-like growth factor (IGF) are upregulated, as a consequence of metabolic changes in response to insulin. Growth of cells, especially tumour cells, which utilise glucose, is promoted.
- Hormone-dependent cancers, such as those of the breast and prostate, are promoted due to the conversion of androgens to oestrogens in adipose tissue.

It is very difficult to separate the effects of obesity from those of dietary factors that may have contributed to the obesity but at the same time also had a promoting effect on cancer development themselves. Nevertheless, weight loss and physical activity may be beneficial as preventive measures against cancer development in overweight subjects.

Other consequences of obesity
These are listed in Table 57.1 and relate to:
- The physical consequences of excessive weight on the skeleton and joints
- The consequences of increased effort by the respiratory muscles required to overcome resistance in breathing
- The consequences of higher body fat levels for anaesthesia and ventilation during surgery
- Poor peripheral circulation, resulting in slower wound healing
- Social consequences of overweight and obesity in terms of societal perceptions and effects on the formation and maintenance of personal relationships, if there is low self-esteem

These may have profound effects on the quality of life and the social experience of the affected individual and may have serious implications for levels of morbidity.
Overweight and obesity: Insulin resistance and metabolic syndrome

Aims
1. To consider insulin resistance as a major metabolic abnormality
2. To describe the metabolic syndrome and its diagnostic criteria

Metabolic effects of obesity
Insulin resistance (and possibly glucose intolerance/type 2 diabetes), dyslipidaemia and hypertension are the major metabolic consequences of obesity. Their coexistence characterises the metabolic syndrome (also known as insulin resistance syndrome or syndrome X). Generally, the syndrome is prodromic for (i.e. leads on to) type 2 diabetes mellitus.

Insulin resistance
The normal function of insulin is to act overall as an anabolic hormone, by targeting a number of tissues and either promoting storage of nutrients or preventing their catabolism (Figure 58.1).

Insulin levels normally rise after meals as glucose concentrations rise and are low in the postprandial state, when stored metabolites are used for energy.

When the response to insulin is muted, the condition is termed insulin resistance. In such subjects, a higher plasma level of insulin is required to achieve the same level of glycaemic control as in a normal subject.

Because insulin has a range of actions, resistance may affect all or only some of these, complicating the clinical picture.

Agreed criteria for diagnosis of metabolic syndrome

- Central obesity, with waist circumference above cut-off level for men (94 cm) and women (80 cm) (European figures)
- These also include two of the following:
  - Raised serum triglycerides (above 1.7 mmol/L)
  - Low high-density lipoprotein (HDL) levels (below 1.03 and 1.29 mmol/L for men and women, respectively)
  - Systolic blood pressure above 130 mmHg, diastolic blood pressure above 85 mmHg or treatment for hypertension
  - Fasting plasma glucose above 5.6 mmol/L or type 2 diabetes diagnosed

Benefits of weight loss
It is estimated that a 10% weight loss can achieve:
- Blood pressure: reduction by 10 mmHg
- Fasting blood glucose: reduction of up to 50% in newly diagnosed patients
- Insulin levels and sensitivity: 30% lower fasting insulin levels and 30% increase in sensitivity
- Progression to diabetes: 40–60% fewer developing diabetes
- Lipids: fall of 10% in total cholesterol, 15% in low-density lipoprotein (LDL) cholesterol and 30% in triacylglycerols (TAGs) and 8% increase in HDL cholesterol
- Mortality: 20% less from all causes and 30% less from diabetes-related disease

Features of insulin resistance
Mechanisms for insulin resistance have been studied extensively in animals, and findings include failure of second messenger signalling, presence of antagonists, a defect in a single cellular enzyme or cellular satiety due to overload with carbohydrate or fat.

However, in humans, it appears that over 75% of insulin resistance is attributable to obesity and low physical fitness.

The key elements of the metabolic abnormality are shown in Figure 58.2 and can be summarised as follows:
- Insulin resistance results in a muted inhibition of lipolysis of stored fat, with larger amounts of non-esterified fatty acids (NEFAs) released into the circulation. This is particularly detrimental in the visceral area, where the NEFAs arrive quickly in the liver via portal blood. It is for this reason that abdominal obesity is particularly involved.
- The NEFAs stimulate TAG synthesis in the liver and the release of very-low-density lipoproteins (VLDLs) into the circulation.
- Elevated VLDLs exchange TAGs with HDLs and LDLs, in exchange receiving cholesterol esters, producing small dense HDL.
- TAG-rich HDLs are broken down by hepatic lipase, resulting in a reduction in levels of HDLs in the circulation.
- TAG-rich LDLs also lose some of their TAGs in the liver by the action of hepatic lipase, becoming denser, due to a relative increase in the proportion of protein. These small dense LDLs are believed to be the most atherogenic lipoprotein particles and thus contribute to increased CVD risk.
- Clearance of chylomicrons and VLDLs from the circulation is also reduced as activity of lipoprotein lipase (LPL) in adipose tissue is insulin dependent. Persistence of these lipoprotein fractions contributes to dyslipidaemia.
- The circulating fats are eventually deposited in tissues, resulting in pathological alterations. Deposits can occur in adipose tissue, in hepatocytes and in skeletal muscle.

In addition to the above effects on fat metabolism, other consequences of insulin resistance include:
- High NEFA levels also inhibit glucose uptake and metabolism in tissues, resulting in hyperglycaemia. This in turn promotes increased insulin release, resulting in hyperinsulinaemia.
- Raised levels of insulin may independently activate the sympathetic nervous system activity and the hypothalamic–pituitary axis, resulting in hypertension.
Figure 58.1 Main actions of insulin under normal conditions

Regulates:
• Fatty acid oxidation
• Cholesterol synthesis
• Glucose storage

Figure 58.2 Consequences of insulin resistance for fat metabolism

* Key atherogenic factors
Aims
1. To consider ways of preventing overweight and obesity
2. To describe options to achieve weight loss and its long-term management

Prevention
Obesity has a multifactorial aetiology (discussed in Chapter 56), which should be addressed at various levels (Table 59.1).

Despite a clear understanding of what needs to be done, these approaches have not achieved the expected success. Reasons might include:
- Under-resourcing for individual action
- Inadequate monitoring of effectiveness
- Little surveillance to trigger early action on weight gain
- Insufficient coordination of initiatives
- Lack of understanding and treatment of underlying causes (e.g. psychological)
- Lack of cultural appropriateness

Non-surgical treatment
First-line treatment for overweight and obesity should be a weight management programme designed to:
- Help overweight individuals lose weight
- Maintain this weight loss with appropriate changes to lifestyle and behaviour
- Achieve a reduction in risk factors

These programmes may be offered in primary care, by local dietitians or commercial slimming groups and health clubs.

A diet and lifestyle approach should be used, combining:
- Dietary measures
- Behaviour change
- Increased activity
- Psychological counselling

Dietary measures are based on healthy eating principles. These are discussed further in Chapter 60.

All dietary recommendations should be discussed with the individual and negotiated to take into account likes and dislikes to maximise compliance. Additional help may include:
- Shopping lists and menu plans.
- Diet plans.
- Fat content may be counted or specific points allotted to foods.

These are all techniques that may help with compliance and will suit particular individuals, but not others.

There are also many other 'slimming diets' available for consumers, discussed in Chapter 60.

Table 59.1 Approaches to prevention of overweight and obesity at the personal and societal levels.

<table>
<thead>
<tr>
<th>Prevention at individual level</th>
<th>Prevention at community/policy level: Action needed to facilitate individual change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modify food choices to be healthier</td>
<td>Policies on labelling/easy availability of healthier choices</td>
</tr>
<tr>
<td>Reduce total energy intake to match output: moderate portion sizes</td>
<td>Food industry action on smaller portions</td>
</tr>
<tr>
<td>Regulate snacking/choose healthier snacks/drinks</td>
<td>Limit advertising of less healthy snacks, especially to children</td>
</tr>
<tr>
<td>Engage in more physical activity, reduce sedentary activities</td>
<td>Encourage walking/cycling and sport by attention to the environment, transport policies and safety measures on roads and in urban spaces</td>
</tr>
<tr>
<td>Early awareness of a need for action on weight</td>
<td>Policy of monitoring weight in children; availability of health checks and accessible evidence-based advice on weight management, with support Regulation of poor-quality/unsound advice</td>
</tr>
</tbody>
</table>

Behaviour change techniques include:
- Setting realistic goals: overambitious targets are likely to be demotivating. These may be weekly or monthly rates of loss, a percentage of current weight or simply stabilisation, with no further gain.
- Support from family and friends: may also occur by a group or programme leader and include support to overcome obstacles and setbacks.
- Anticipating the barriers to progress: may include keeping a diary to identify triggers to eating, coping with difficult situations and establishing self-belief for success.

Physical activity provides an additional means of achieving a negative energy balance:
- In conjunction with dietary measures, activity contributes to weight loss and protects the lean body mass. This helps to maintain the metabolic rate, which decreases when energy intake is reduced.
- Vigorous activity also results in a post-exercise elevation of metabolic rate, further enhancing energy utilisation.
- Activity can increase fat utilisation and sensitivity to insulin and improve blood lipid profiles.
- Activity induces a feeling of well-being, which can improve the mood and self-image of an individual on a weight loss programme.
- Increased mobility and lung function may be additional benefits.
- Exercise on prescription, and referral to weight loss programmes and slimming groups, is becoming accepted within primary care.
Drug treatment

There are specific guidelines on the use of anti-obesity drugs. Individuals should also have appropriate advice on diet and physical activity with behavioural strategy support.

There are a large number of over-the-counter formulations that claim to promote weight loss, but most of these have not been adequately evaluated for efficacy or safety.

Surgical treatment (bariatric surgery)

This approach is only used in cases of morbid obesity (BMI >40 or 35–40 kg/m² with comorbidities such as cardiovascular disease, metabolic disorders, severe psychological conditions related to diet). Two types of surgical intervention are used (Table 59.2):

• Restrictive surgery: designed to reduce the size and capacity of the stomach and induce an earlier feeling of satiety
• Malabsorptive surgery: designed to reduce the area of the small intestine available for absorption

With careful management before and after the procedure, outcomes are more favourable compared to non-surgical treatment, including greater reduction of body weight, waist circumference and plasma concentrations of triglyceride and glucose and greater chance of remission of diabetes and metabolic syndrome. However, the long-term benefit of bariatric surgery is currently not well examined. Appropriate consistent follow-up arrangements must be available for patients to manage complications. Malabsorption conditions arising from bypass operations are associated with nutritional deficiencies and require supplementation. The process of surgical treatment of obesity (pre- and post-operation and long-term follow-up) must therefore involve an interdiscipliary health-care team including physician, surgeon, psychologist, dietitian, nurse and social worker. Some examples of nutritional management for post-operative care include:

• Increased daily protein intake of 90–120 g to maintain lean body mass
• Long-term vitamin and mineral supplementation to compensate possible reduced uptake and absorption
• Continuous reinforcement of healthy dietary habits

Table 59.2 Overview of currently used surgical interventions for morbid obesity.

<table>
<thead>
<tr>
<th>Name of treatment</th>
<th>Procedure</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malabsorptive surgery</td>
<td>Sections of GI tract bypassed to reduce surface area for absorption</td>
<td>Weight loss substantial and maintained</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metabolic complications include vomiting, stenosis, dumping syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients need to be monitored</td>
</tr>
<tr>
<td>Jejunoileal Gastric bypass Biliopancreatic diversion</td>
<td>Bypasses a large area of small intestine (SI)</td>
<td>High risk of complications; rarely performed</td>
</tr>
<tr>
<td></td>
<td>Reduces stomach size and bypasses the duodenum</td>
<td>Reduced capacity and digestion</td>
</tr>
<tr>
<td></td>
<td>As above, but the jejunum also bypassed</td>
<td>More extensive effect on absorption</td>
</tr>
<tr>
<td>Restrictive surgery</td>
<td>Reduces the size of the stomach</td>
<td>Limits capacity for food, but not absorption</td>
</tr>
<tr>
<td>Gastroplasty</td>
<td>The stomach divided to make a smaller pouch (vertical division more successful)</td>
<td>Less weight loss than with gastric bypass</td>
</tr>
<tr>
<td>Gastric banding</td>
<td>Constricting band around the stomach limits capacity, may be adjusted to vary extent of restriction</td>
<td></td>
</tr>
</tbody>
</table>
Overweight and obesity: Popular slimming diets

Aims

1. To identify the criteria relating to a safe diet designed for weight loss
2. To consider the types of commercially available diets for weight loss

The media promote ‘diets’, which are invariably focused on weight loss, such that the term ‘diet’ is synonymous in the public mind with eating less to achieve weight reduction. This is in contrast to the nutritionists’ view that ‘diet’ refers to an individual’s food intake.

The slimming industry

For many people, a slow and steady weight loss seems unsatisfactory, and ‘quick fix’ regimes are sought. In addition, those who have regained weight may look for a new approach. As a result, an ever-changing industry of slimming programmes has grown to fill this need. A poorly balanced slimming regime may lead to nutritional deficiencies.

Criteria for a nutritionally sound and safe slimming regime

A slimming regime should fulfil a number of criteria (Table 60.1) to be considered sound.

Healthy eating guidelines can underpin dietary advice for weight loss in a number of ways. These are summarised in Table 60.2.

Table 60.1 Summary of criteria for a nutritionally sound and safe weight loss regime.

<table>
<thead>
<tr>
<th>Criterion to be fulfilled</th>
<th>Explanation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritionally balanced</td>
<td>No major food groups should be excluded or eaten to excess; principles that underpin healthy eating should be evident</td>
<td>Avoids risk of deficiency or need for supplements</td>
</tr>
<tr>
<td>Biologically plausible</td>
<td>Should not make claims that run against known biological facts</td>
<td>May be difficult for consumer to recognise</td>
</tr>
<tr>
<td>Safe</td>
<td>Must not recommend levels of intake that endanger health</td>
<td>Should carry advice to check with doctor</td>
</tr>
<tr>
<td>Realistic</td>
<td>Results promised should be realistic</td>
<td>Misleading claims will be demotivating</td>
</tr>
<tr>
<td>Flexible</td>
<td>Diet should allow some personal choices to maintain motivation</td>
<td>Rigid eating regimes lead to abandonment</td>
</tr>
<tr>
<td>Sustainable</td>
<td>Diet should fit as much as possible into normal life; eating special and unusual foods may be a novelty, but does not fit easily into social existence</td>
<td>Special items increase costs and highlight ‘dieting behaviour’</td>
</tr>
<tr>
<td>Physical activity</td>
<td>A sensible amount should be recommended to support dietary regime</td>
<td>Can improve self-image and help towards successful outcome</td>
</tr>
</tbody>
</table>

Table 60.2 Basic measures underpinning dietary advice for weight loss.

<table>
<thead>
<tr>
<th>Dietary measure</th>
<th>Target change</th>
<th>Reasons for change/gain to be made</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in total energy</td>
<td>2.4 MJ (600 kcal) or a 2–4 MJ (500–1000 kcal) deficit</td>
<td>To produce a negative energy balance</td>
</tr>
<tr>
<td>Lower total fat intake</td>
<td>To a moderate level</td>
<td>Monounsaturated fats should predominate</td>
</tr>
<tr>
<td>Starchy foods should be maintained</td>
<td>Include those with a lower glycaemic index</td>
<td>Maintain a steady blood glucose level, and avoid periodic hunger; a higher non-starch polysaccharide (NSP) intake will promote satiety</td>
</tr>
<tr>
<td>Fruit and vegetables</td>
<td>At least five a day</td>
<td>Provide micronutrients and low-energy, nutrient-dense intake. Useful snacks</td>
</tr>
<tr>
<td>Soft drinks</td>
<td>To be avoided</td>
<td>Provide energy and promote passive overconsumption</td>
</tr>
</tbody>
</table>

Types of slimming diets

Various approaches are used by the slimming industry, from ones that are safe and based on good principles to others that can be viewed as potentially dangerous or at least misleading (Table 60.3):

1. Sensible healthy eating plans with reduced energy

A number of ‘slimming’ organisations have well-balanced diet plans and use systems such as points or exchanges that allow the individual to adjust their intake in line with a target energy allowance. Some include an exercise regime and provide group support through regular meetings. Generally, these are safe and meet essential criteria.

2. Diets that maintain satiety

The clear way to consume less energy is to eat less, but to ensure that this is acceptable, satiety needs to be maintained. This can be achieved by:

- Increasing intake of all plant foods. These can displace more energy-dense items, especially high-fat products, while providing bulk in the digestive tract, promoting satiety and avoiding hunger. This approach is used in many healthy diet plans and provides a sound framework for weight loss.
- Eating foods with a lower glycaemic index (GI) in place of high-GI foods slows down the absorption of glucose and the release of insulin. It is suggested that the high levels of insulin promote fat storage, making high-GI foods more ‘fattening’. At present, there are insufficient data about the GI effect of mixed diets, as most studies have been done on single foods, so there is currently no evidence that this is a suitable diet to achieve weight loss.
3. Diets that adjust macronutrient content

Low-fat diets. Fat in the diet is more energy dense than other macro-nutrients and is believed to be associated with ‘passive overconsumption of energy’, so reducing the intake of fat is a logical approach to follow. Many low-fat diets exist, where fat intake is 20–30% of total energy, with an increase in the content of complex carbohydrate.

This improves cardiovascular risk factors and may protect from other chronic diseases. Focusing on a reduction in fatty foods allows healthy eating to become established to help in longer-term maintenance. Combining a reduction in the percentage of fat with an overall lowering of energy intake produces better weight loss than simply replacing fat with carbohydrate.

Low-carbohydrate diets. These have been promoted, with the energy being made up from protein and fat. The most famous of these is the ‘Atkins diet’. There is initial rapid weight loss as glyco-gen reserves and the associated water are lost. The lack of carbohydrate for metabolism results in ketosis, which causes nausea, dehydration and bad breath. Constipation is likely because of the low fibre intake.

The high fat intake is contrary to all healthy eating principles. Weight loss does occur, but this is attributed to the anorectic effects of a high-protein diet and the reduced overall energy intake. Low intakes of minerals and vitamins will, if not supplemented, result in deficiency.

4. Diets that prescribe meal composition or timing of meals

Food combining suggests that foods containing proteins should not be eaten with carbohydrate-containing foods, as they cannot be digested simultaneously. There is no scientific evidence for this. Weight may be lost because attention is being paid to what is eaten, and overall food intakes are likely to be reduced as a result.

Consuming foods only before a certain time in the day is proposed by another diet to allow the body to complete digestion before night-time. Again, the main effect of this is to limit overall food intake.

5. Diets that ‘preload’ the digestive system before meals

Eating a fruit before a meal to provide ‘enzymes’ and eating grapefruit to ‘eliminate fat’ are two suggested eating patterns, neither of which have any scientific base. In both cases, the preload is likely to reduce the food eaten at mealtimes.

Drinking water before meals to cause weight loss may promote a feeling of fullness at mealtimes and so reduce food intake. However, water is rapidly absorbed from the stomach, so would have a short-term effect.

6. Diets that avoid supposed ‘allergic reactions’

These invoke claims that overweight is due to an allergic reaction by the body to food components that do not ‘match’, including eating different types of foods depending on blood group, or a mismatch of electric charges between the food and the individual. Both focus on elimination of entire food groups and are nutritionally dangerous without any scientific basis.

7. Diets that require supplements

A variety of these exist that are reported to boost energy, detoxify, improve cellular activity, etc. Unless there are clear medical reasons for poor digestion or absorption, these preparations will not help in weight loss.

8. Eating one food only

There are single-item, very-low-energy diet products that can be used for short-term rapid weight loss. The popular diets that advise consuming a single product, such as cabbage soup, have no nutritional credibility and are unsustainable.

Monotony and boredom restrict intake and the consumer learns nothing about a healthy balanced diet for future weight control. Serious risk of deficiency also exists.

9. Fasting/meal skipping

This may be seen as the easiest way of losing weight, but it is unsustainable and likely to result in a very erratic food intake with the risk of nutritional deficiency. Risks of dehydration in the short term and eating disorders in the longer term are possible.

Weight loss needs to be addressed by a public health approach with a higher rate of success than at present. Meanwhile, vulnerable individuals will continue to be exposed to unsound and unsafe slimming regimes. It would be helpful if at least the awareness of what to look for in a weight reduction programme was more widely recognised.

### Table 60.3 Evaluating types of slimming diets against criteria.

<table>
<thead>
<tr>
<th>Type of diet</th>
<th>Balanced</th>
<th>Plausible</th>
<th>Safe</th>
<th>Realistic</th>
<th>Flexible</th>
<th>Sustainable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy eating plans</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Increasing plant foods</td>
<td>Possible</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Possible</td>
<td>Yes</td>
</tr>
<tr>
<td>Eating low-GI foods</td>
<td>Possible</td>
<td>Little evidence</td>
<td>Yes</td>
<td>Yes</td>
<td>Possible</td>
<td>Yes</td>
</tr>
<tr>
<td>Lower fat diets</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low-CHO diets</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Food combining</td>
<td>No</td>
<td>No</td>
<td>Possible</td>
<td>Possible</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Eating at certain times</td>
<td>Possible</td>
<td>No</td>
<td>Possible</td>
<td>Possible</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Preload before meals</td>
<td>Possible</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Avoiding allergens</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Supplement-requiring diets</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Eating one food only</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Fasting/meal skipping</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

### Principles of weight reduction

The scientific principle of weight reduction is straightforward:

- Energy intake must be less than energy output to create a negative energy balance, resulting in weight loss, as stored fat reserves are used for energy.
- Energy deficits of 500–1000 kcal (2–4 MJ) per day may be recommended, depending on body size and gender.

Weight loss is generally slow, ~0.5 kg/week, unless the energy deficit is great, when there is also likely to be significant loss of lean tissue.

When weight has been lost, the further problem of mainte-nance creates a challenge to individuals, who may gradually regain weight.
Aims

1. To consider reasons for underweight
2. To describe the body’s response to a negative energy balance

A deficit of energy intake, in naturally occurring situations (e.g. famine conditions), is generally accompanied by an inadequate intake of nutrients. There are a number of contributory factors, which may also determine the metabolic consequences and any treatment that is attempted.

The most obvious consequence of the energy deficit is loss of weight, attributable to an imbalance between energy intake (which is reduced) and energy expenditure (which may be increased, unchanged or even reduced from a previous level).

In the majority of instances, there is an adaptive physiological response to minimise energy expenditure when intake is reduced and therefore facilitate survival.

Starvation

This is the most challenging situation, as energy intake falls to zero.

When no food is eaten, the body must adapt to utilise stored energy reserves. The largest of these is body fat, stored in adipose tissue, which can supply fatty acids for energy provision. However, the brain and red blood cells require a supply of glucose to function, and metabolic adaptations must occur to preserve carbohydrate and use it efficiently.

A number of neural and hormonal responses are involved; these include:
- Reduced sympathetic nervous system activity
- Lower levels of active thyroid hormone (T₃)
- Lower levels of insulin
- Leptin activity, which modulates the energy-sparing response

Adaptation to starvation

This develops over a period of time and involves changes to metabolism of substrates:
- Carbohydrate stores, as glycogen in the liver and muscle, are limited and may be completely exhausted within 24 h.
- Hepatic gluconeogenesis can generate glucose de novo, from glycerol (from lipids) and carbon skeletons of amino acids. There is an initial phase, lasting 3–4 days, of protein breakdown from skeletal muscle for energy.
- A fall in circulating glucose and insulin levels stimulates lipolysis; tissues use more fatty acids for energy and glycerol is directed to gluconeogenesis. Ketone bodies are produced by the oxidation of fatty acids in the liver.
- The brain adapts to the use of ketone bodies for energy, meeting some two-thirds of its energy requirements in this way. Small amounts of glucose are produced by gluconeogenesis. This adapted steady state may take up to 3 weeks to establish and can persist as long as fat reserves are available. This tends to be longer in women than in men and depends on the previous level of nutrition. As women have more body fat, this extends the survival period.
- Once fat reserves are depleted, structural proteins are broken down, and there is a rapid deterioration leading to death.

(See Figure 61.1 for a summary of this process.)

Adaptations of energy expenditure

These also occur and therefore contribute to minimising the energy imbalance:
- Resting metabolism – there is an early phase of increased metabolic efficiency; later metabolism uses less energy as a result of a smaller mass of active tissue.
- Thermogenesis – where no food is consumed, there will be no diet-induced thermic response; undernourished individuals have been shown to have a poorer thermogenic response on exposure to cold.
- Physical activity – observations of individuals who are starving, or in negative energy balance due to undernutrition, show that
Chronic energy deficits

For a large percentage of the population in the less developed countries of the world, chronic energy deficiency is a permanent feature of life. The adaptations that occur enable the body to survive but often at a cost to long-term health.

Energy deficit compounded by disease or trauma

The concurrence of a metabolic response to disease or trauma with energy deficit is likely to exacerbate the negative energy balance for a number of reasons:

- Injury, infection and fever increase the metabolic rate, in proportion to the extent of the physiological stress.
- Protein is catabolised from muscle for the production of acute-phase proteins by the liver, and nitrogen losses increase.

- The major hormones of the stress response are cortisol and catecholamines, which stimulate glucose production and increase energy expenditure.

This metabolic response may result in a serious loss of weight in an undernourished patient which, together with tissue wasting and anorexia, results in cachexia, with a high risk of mortality. This can occur in some chronic illnesses. The need for nutritional support must be assessed, and appropriate measures quickly introduced. This can be a major problem in hospital patients.

Causes of reduced energy intake

These might include:

- Poor food availability
- Inability to eat due to illness or following injury or trauma
- Intentional/deliberate restriction of food, either for a short term (e.g. to lose weight) or as a long-term behaviour (possibly associated with some form of eating disorder) or a political statement

Causes of increased energy expenditure might include:

- Heavy manual labour or physical activity
- Increased requirements for growth
- Fever/infection/post-traumatic response
Aim

To describe the possible factors in the diet that may have a causative role in cancer

One in three people will be diagnosed with cancer in their lifetime. Specific types of cancer vary in prevalence in different parts of the world. This difference reflects the variety of environmental factors, including diet, that play a role in causation.

There is a growing burden of cancer deaths worldwide, associated with an ageing population. However, there are also differing trends in the rates of some cancers. For example, in the West, lung cancer rates have been falling in men but increasing in women, as smoking behaviours change. In Japan, there has been a rapid increase in colorectal cancer rates during the last 30 years, as diets become more Westernised.

What is cancer?

Cancer is a disorder of somatic cells, in which changes to the genetic material cause a normal cell to behave abnormally in form or function. The change that occurs may be inherited or may occur sporadically. The result is that the cell fails to function as it should, in not responding to regulatory signals that control its life cycle. As a result, it may divide inappropriately or fail to die (apoptose) at the end of its life cycle, with the result that a cluster of cells is eventually produced, forming a tumour.

Stages in the development of cancer have been identified, and mechanisms within these are still being studied. However, it is clear that movement through the stages is not inevitable, and repairs can be made that stop or slow down the process.

It is within these ‘accelerating’ or ‘braking’ mechanisms that the environment and diet can play a role. These are summarised in Figure 62.1.

Evidence on causation of cancer

A number of environmental factors, including diet, have been associated with the aetiology of cancer. However, providing sound evidence is sometimes difficult:

- Much evidence is based on epidemiological studies of populations (see Chapters 30 and 31), allowing the calculation of the relative risk of the disease, based on levels of exposure to a causative factor (e.g., diet). Epidemiology cannot provide proof of cause and effect, and associations may be confounded by other differences between populations. Studies of migrants who develop rates of cancer typical of their host country within a generation confirm the importance of environment.

- Case–control studies provide further information about exposure to causative factors, but the time course of cancer development can blur the relationship between exposure and diagnosis of cancer. Trials of interventions with putative preventive factors have been disappointing and have failed to confirm the protective roles of nutrients such as β-carotene or vitamin E. Reasons for this may include the use of a single nutrient supplement rather than whole food sources and the timing of the interventions.

- Very-large-scale prospective cohort studies are now under way, such as the European Prospective Investigation into Cancer and Nutrition (EPIC) \((n = 500\,000)\) and the Multiethnic Cohort (MEC) \((n = 215\,000)\), which have recruited participants who are being followed up, to identify cancer development and link this with earlier exposure to risk factors. Smaller cohort studies provide some evidence on diet and environmental associations, but with homogeneous cohorts, there are limits to the general application of the results.

- Findings from population studies are gradually being tested in experimental situations to elucidate mechanisms. For example,
an association between red meat intake and bowel cancer, observed by the EPIC study, has been tested experimentally. This has demonstrated that red meat consumption causes N-nitroso compound levels in faeces to increase and that there is an increase in DNA mutations of colonic cells with higher levels of these compounds.

**Diet as a factor in cancer**

It is estimated that an average of 30% of cancer is diet related: this ranges from a low level for lung cancer to 80% for colorectal cancer.

Difficulties in attributing causation to dietary factors occur because:

- Diets are extremely complex, and particular nutrients can occur in many different foods.
- Certain aspects of the diet co-vary in individuals, such that a high intake of one food, for example, meat, may be associated with a low intake of fruit and vegetables.
- Patterns of food intake obtained from food frequency questionnaires may not be sufficiently specific to demonstrate differences and relationships.
- Dietary records may contain errors, but more robust techniques are being developed that cross-check dietary records with blood concentrations and other biomarkers.

Nevertheless, information about the roles of diet suggests that it can:

- Be a source of preformed carcinogens or precursors (i.e. compounds that can be converted into carcinogens)
- Contain nutrients that affect the formation, transport, deactivation or excretion of carcinogens
- Contain nutrients that can be protective, by promoting the body's resistance to carcinogens and therefore increasing the resistance of cancer

Some evidence exists of a promoting effect of certain dietary factors in cancer (Table 62.1).

Avoidance of these foods or dietary components may help protect individuals against the development of cancer and should feature in advice (see Chapter 63).

<table>
<thead>
<tr>
<th>Food or nutrients</th>
<th>Possible role in cancer promotion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy intake</td>
<td>High energy intakes result in overweight and obesity, linked to greater incidence of hormone-related cancers: breast, endometrium and prostate. Also a positive association with cancers of the oesophagus, colorectum, pancreas and kidney</td>
</tr>
<tr>
<td>Fat intakes</td>
<td>Difficult to separate from the evidence on overweight. High fat intakes (especially of saturated fat) have been associated with lung, colorectal, prostate and breast cancers</td>
</tr>
<tr>
<td>Alcohol</td>
<td>May potentiate the role of other carcinogens, increasing uptake or susceptibility of cells</td>
</tr>
<tr>
<td>Salt</td>
<td>Linked with gastric cancer; high levels of salt reduce gastric acidity, which in turn promotes conversion of dietary nitrates to nitrites and nitrosamines, which are carcinogenic</td>
</tr>
<tr>
<td>Meat</td>
<td>Metabolic products in the colon arising from digestion of red meat are N-nitroso compounds, which have been found to cause DNA mutations. Thus, there is a possible mechanism for development of colorectal cancer. Processed meat and charred meat may also contribute by forming heterocyclic amines, which are broken down to carcinogenic products</td>
</tr>
</tbody>
</table>
Aims
1 To describe possible factors in the diet that may have a protective role in cancer
2 To formulate dietary advice for prevention of cancer

Protective effects against cancer can be obtained from foods and nutrients, which act to repair damage or prevent promotion and subsequent progression to tumour development (Table 63.1).

Summary of evidence on diet and cancer
Although conclusive evidence of cause and effect from dietary factors is largely lacking in the causation of cancer, there is a substantial body of evidence that points to relationships between dietary components and increased or reduced risk. It should also be recognised that maintenance of physical activity and not smoking are key lifestyle guidelines that should be adhered to. These are summarised in Table 63.2 for the most common cancer sites.

There is evidence of a possible association for other sites and other dietary factors, but this at present is insufficient.

Advice on diet and lifestyle
The current evidence on cancer suggests that dietary change is important.

Following healthy eating guidelines, with particular attention to the following aspects, forms the cornerstone of dietary prevention of cancer:

• Maintenance of normal body weight
• Physical activity according to guidelines (at least 30 min on 5 days per week)
• At least 400 g/day of fruit and vegetables, including a variety of types
• Increased intake of plant foods rich in complex carbohydrates, for example, grains, cereals and pulses, to provide the main source of energy
• Minimal alcohol consumption
• Reduced intakes of red meat, fat and salt
• Avoidance of salt‐preserved and processed foods
• Safe food preparation: avoidance of foods that are spoilt or potentially contaminated with moulds or bacteria.

Table 63.1 Dietary factors with a possible protective role in cancer.

<table>
<thead>
<tr>
<th>Food or nutrients</th>
<th>Possible role in protection against cancer</th>
</tr>
</thead>
</table>
| Non‐starch polysaccharides (dietary fibre) | Diets high in fibre confer some protection against colorectal cancer This may be effected in a number of ways:  
  • More rapid removal of potential carcinogens by faster transit through the bowel  
  • More beneficial nutrients available for the colonocytes  
  • Healthier bacterial flora in a more acidic environment  
| Fruit and vegetables | There is consistent evidence that diets high in fruit and vegetables are associated with lower cancer rates and no evidence to the contrary  
  It is believed that the antioxidants supplied by these foods play a protective role against damage to DNA and other molecules  
  Other substances contained in fruit and vegetables may be important: these include various phytochemicals such as flavonoids, phytosterols, isothiocyanates, sulphur‐containing compounds and phyto‐oestrogens. A wide range of fruit and vegetables must be eaten to incorporate all of these |
| Folic acid | Evidence suggests that higher intakes of folate are associated with lower risk of cancer, particularly of the pancreas. The mechanism appears to be a protection against mutations of DNA |
| Calcium and vitamin D | An inverse relationship between calcium intake (as dairy products) and colon cancer has been reported. This may be due to binding in the gut of fats by calcium, thus reducing potential harm from fats and bile acids. However, a positive association has been reported between high intake of calcium and increased risk of prostate cancer  
  Vitamin D may have an anticancer action in its own right and has been proposed to reduce risk of colon cancer |
<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Convincing/probable evidence of decreased risk</th>
<th>Convincing/probable evidence of increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerodigestive system</td>
<td>Fruit and vegetables</td>
<td>Alcohol, smoking, tobacco</td>
</tr>
<tr>
<td>Stomach</td>
<td>Non-starchy vegetables, <em>Allium</em> vegetables and fruit</td>
<td>Salt, salted and salty foods</td>
</tr>
<tr>
<td>Colorectum</td>
<td>Physical activity, foods containing fibre, calcium, milk and garlic</td>
<td>Overweight/obesity, red and processed meat, total fat, alcoholic drinks, body fatness, abdominal fatness and adult attained height</td>
</tr>
<tr>
<td>Liver</td>
<td>Fruits, foods containing carotenoids</td>
<td>Aflatoxins and alcohol</td>
</tr>
<tr>
<td>Lung</td>
<td>Lactation and physical activity</td>
<td>Arsenic in drinking water and β-carotene supplements and smoking</td>
</tr>
<tr>
<td>Breast</td>
<td>Foods containing folate</td>
<td>Alcohol, obesity, adult attained height</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Physical activity</td>
<td>Body fatness, abdominal fatness and adult attained height</td>
</tr>
<tr>
<td>Ovary</td>
<td>Foods containing lycopene and selenium</td>
<td>Adult attained height</td>
</tr>
<tr>
<td>Endometrium</td>
<td></td>
<td>Body fatness, abdominal fatness</td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td>Diet high in calcium</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td>Body fatness</td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td>Arsenic in drinking water</td>
</tr>
</tbody>
</table>

Adapted from American Institute for Cancer Research 2007.
Diet and cardiovascular disease: Aetiology

Aims
1. To describe the development of cardiovascular disease
2. To identify the major risk factors involved in the aetiology of the disease

Definitions
Cardiovascular disease (CVD) includes coronary heart disease (CHD), cerebrovascular disease and peripheral vascular disease (PVD). All share the common features of thickening and hardening of the arterial walls resulting in a compromised blood flow.

Mortality rates
CVD is the leading cause of death in the developed world and accounts for approximately one-third of all deaths worldwide. Deaths from CHD comprise about half of the total and stroke deaths a further quarter:
- In general, death rates due to CVD are higher in industrialised countries but with substantial variation.
- In recent decades, death rates from CVD in many Westernised countries have been falling, but developing countries are experiencing rapid increases in these diseases as they undergo economic and nutritional transition.

Pathology
The fundamental lesion is the atherosclerotic plaque that develops within the arterial wall and its eventual rupture. These processes occur slowly and over a prolonged period.

The three main stages in the process are summarised in Figure 64.1:
1. The vascular endothelium is the key surface at which several contributory factors interact. The endothelium has many self-regulating properties, achieved through the production of nitric oxide, prostacyclin and other bioactive substances. Many of the risk factors cause dysfunction here. As a consequence, the endothelium becomes more permeable to lipids and proteins.
2. Low-density lipoproteins (LDLs) in the blood readily pass into the arterial wall to deliver cholesterol to the tissues. If they become oxidised, the cascade of events results in the formation of atherosclerotic plaque.

3. If the plaque becomes unstable and ruptures, activation of platelets and the blood coagulation cascade can result in clot formation (thrombosis) and a myocardial infarction (or ischaemic stroke in the case of its occurrence in the brain).

Risk factors for CVD
The pathological process comprises many elements, which may be exacerbated or ameliorated by ‘risk factors’.

Two categories are identified: irreversible and potentially modifiable (behavioural) (see Figure 64.2).

Irreversible risk factors
- Genetic traits – include disorders of lipid metabolism.
- Male gender – higher risk than in premenopausal women; risk equalises later in life.
- Increasing age – progressive increase of risk.
- Lower socioeconomic status – associated with higher risk.
- Ethnicity – higher risk in some ethnic groups (e.g. from Indian subcontinent).
- Small for gestational age at birth – greater risk in later life.

Modifiable (behavioural) risk factors
These are related to diet and lifestyle factors and have been the focus of health education initiatives for many years. Many of these risk factors overlap, either in their consequences or in the causative factors (Figure 64.2).

Many of the risk factors have dietary components that contribute to or minimise the disease process. These are discussed further in Chapter 65:
- Smoking – contributes to endothelial dysfunction and increases oxidative stress, promoting oxidation of LDLs.
- Physical activity – an increased level of activity reduces the impact of many other risk factors. For example, physical activity reduces obesity, which is associated with insulin resistance, hypertension and abnormal blood lipids. Lipid profiles are normalised (including an increase in HDL levels), endothelial function and clotting-related factors are improved, and markers of inflammation decrease.

Modifiable risk factors offer an opportunity for intervention by health professionals, both as general health education and as targeted individual advice, to reduce the eventual risk of developing CVD. If CVD is already present, then more intensive advice or secondary prevention may be necessary.
Chapter 64  Diet and cardiovascular disease: Aetiology

Atherosclerotic plaque Leading to the development of an
Damaged endothelium becomes more permeable
Pathological process
Accumulation of LDL and cholesterol
Free radicals oxidise LDL and are scavenged by macrophages forming foam cells
Release of cytokines – low-grade inflammatory response
Accumulation of smooth muscle cells Ca$^{2+}$ and fatty deposits

Irreversible Modifiable
• Male
• Increasing age
• Genetic predisposition
• Ethnicity

Modifiable
• Smoking
• Physical activity
• Hypertension
• Dyslipidaemia
• Obesity
• Type 2 diabetes
• Blood coagulability
• Raised homocysteine

Consequences of reduced blood flow
• Angina pectoris
• Myocardial infarction
• Cerebral ischaemia–stroke
• Claudication

Disease state
• CHD
• Cerebrovascular disease
• Peripheral vascular disease

Figure 64.1  Summary of the risk factors, pathological process and consequences of the atherogenic process

Figure 64.2  Interactions between the major modifiable risk factors for CVD

Smoking Reduced physical activity Low fruit and vegetable intake

Hypertension Obesity Raised lipid levels

↑ Blood coagulability
Type 2 diabetes

↓ Antioxidant status
↑ Homocysteine levels

All leading to an increased risk of developing CVD
Diet and cardiovascular disease: Prevention

Aims
1. To describe the evidence for the dietary factors involved in each stage of the development of cardiovascular disease
2. To use this evidence to formulate practical dietary advice

The aetiology of cardiovascular disease (CVD) is multifactorial, with a number of risk factors influencing the development and progression of the disease. From an understanding of the pathology of CVD (see Chapter 64), it is possible to identify dietary components that either contribute to or help to prevent the disease process. Although incomplete, current knowledge is used to advise on diets that reduce CVD risk.

Endothelial dysfunction
There is no ‘gold standard’ measurement for endothelial function, but vasodilatory capacity and assay of endothelium-derived products in plasma and urine are used as proxy indicators of function.

Many of the factors that affect the endothelium (see Table 65.1) also influence other stages of the pathological process.

Blood lipids
The quantity and composition of dietary fats are recognised as key determinants of the plasma lipid profile:
• Persistently elevated triglyceride levels alter the normal exchange of constituents between lipoprotein fractions, resulting in the formation of small dense LDLs and HDLs, which promote atherogenesis.
• Modifications to the proportions of consumed fats have been at the core of advice regarding dietary prevention of CHD since the 1970s.

The goal is to achieve reductions in total cholesterol, particularly that in the LDL fraction, and an increase in HDL levels. This advice reflects developments in knowledge and is summarised in Table 65.2.

Oxidative stress
The oxidation of LDL particles is a key stage in the pathology of CVD. LDL particles contain large amounts of polyunsaturated fats, which are vulnerable to oxidation. Markers of oxidative stress are increased in CVD.

Antioxidants are also present within the LDLs and can provide some protection against free radicals. The diet is an important source of exogenous antioxidants:
• Fruit and vegetables are the main dietary sources of antioxidants, and populations in which there is a high level of consumption of these foods have a reduced risk of CVD. An inverse association has been shown between plasma levels of antioxidants, including ascorbate and vitamin E, and CVD risk. However, intervention trials, using individual antioxidant vitamins alone or in combination, have failed to show evidence of benefit and in some cases produced negative outcomes.
• Plant foods contain many other compounds with antioxidant activity (e.g. flavonoids), but more information is needed about their precise chemical forms and concentrations in foods, their bioavailability and metabolism within the body and the likely plasma and LDL concentrations that can be reached when these foods are eaten before any conclusions can be drawn about their role as protective agents against CVD. Current advice is to focus on foods rather than specific dietary components and to increase consumption of fruit and vegetables to at least five portions (or 400 g) per day, thereby providing a range of antioxidants.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Suggested mechanism</th>
<th>Strength of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary fat intake</td>
<td>Elevated levels of TAG-rich lipoproteins after meals have a pro-oxidant effect on the endothelium and may impair vasodilation</td>
<td>Consistent for harmful effect of atherogenic lipaemia</td>
</tr>
<tr>
<td>Fish oils</td>
<td>Especially docosahexaenoic acid (DHA), incorporated into membrane phospholipids, attenuates proinflammatory and prothrombotic activity</td>
<td>Evidence is consistent for reduction in fatal CHD</td>
</tr>
<tr>
<td>Antioxidant nutrients</td>
<td>Protect against free-radical damage, for example, resulting from hypertension, smoking and pro-oxidant products</td>
<td>Consistent evidence from laboratory and in vivo studies; benefits not shown in intervention trials</td>
</tr>
<tr>
<td>B vitamins and folate</td>
<td>Reduction of homocysteine (HCys) levels in circulation. HCys is believed toxic to endothelium, possibly through reduced response to acetylcholine</td>
<td>Reduction in vascular events in treatment groups and improved ECG; large trials of supplementation awaited</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Increases HDL levels, which act as antioxidants. May also have anti-inflammatory effect</td>
<td>Moderate intakes lower CHD</td>
</tr>
</tbody>
</table>
Table 65.2 Practical advice on dietary fats to modify plasma lipids and the origins of such advice.

<table>
<thead>
<tr>
<th>Dietary lipid</th>
<th>Effect on plasma lipids</th>
<th>Practical application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat</td>
<td>High-fat diets generally associated with high CHD rates.</td>
<td>Fat reduction to 20–35% of total energy is widely recommended</td>
</tr>
<tr>
<td></td>
<td>Low-fat diets are shown to reduce LDL levels</td>
<td>More substantial reduction may limit compliance and may result in high CHO intakes,</td>
</tr>
<tr>
<td></td>
<td>However, replacement of fat with CHO may increase TAG levels; the effect can be</td>
<td>which increase VLDL levels</td>
</tr>
<tr>
<td>SFAs</td>
<td>counteracted with physical activity</td>
<td>Reductions in dietary sources of SFA generally agreed;</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>SFAs with 14 and 16 carbons are particularly strongly related to raised LDL levels.</td>
<td>target intakes normally 10% of total energy</td>
</tr>
<tr>
<td></td>
<td>Reduction in SFA intake reduces total cholesterol, LDL and HDL (less than LDL);</td>
<td></td>
</tr>
<tr>
<td></td>
<td>effects on CHD well supported with evidence</td>
<td></td>
</tr>
<tr>
<td>n-6 PUFAs</td>
<td>Increases levels of plasma cholesterol to varying extent in individuals. Absorption</td>
<td>Closely associated with SFA in the diet, and emphasis on reducing SFA also limits intake of cholesterol</td>
</tr>
<tr>
<td></td>
<td>from diet is limited</td>
<td>Eggs are cholesterol rich and intake may need to be controlled in susceptible individuals</td>
</tr>
<tr>
<td>MUFAs</td>
<td>Replacement of SFAs with n-6 PUFAs reduces LDL levels, with little change to HDL levels,</td>
<td>Intakes above 10% of energy not recommended due to risk of peroxidation of double bonds</td>
</tr>
<tr>
<td></td>
<td>resulting in improved lipid profile. May also help clearance of VLDLs in</td>
<td></td>
</tr>
<tr>
<td></td>
<td>postprandial state</td>
<td></td>
</tr>
<tr>
<td>Trans-fatty acids</td>
<td>Cause an increase in LDLs and reduce HDL levels, potential to contribute to CHD</td>
<td>Levels should be kept as low as possible;</td>
</tr>
<tr>
<td>n-3 PUFAs</td>
<td>Reported to improve the clearance of VLDLs from circulation and lower concentrations</td>
<td>Effects on lipid clearance seen at high doses only, greater than can be achieved</td>
</tr>
<tr>
<td></td>
<td>of small dense LDLs</td>
<td>with oily fish</td>
</tr>
</tbody>
</table>

Inflammation

An inflammatory state appears to exist in CVD, probably resulting from a generalised response to local factors associated with the atherosclerotic plaque.

Key indicators of this response are raised levels of C-reactive protein (CRP) and fibrinogen:
- **Obesity** is associated with raised levels of CRP, and levels fall on weight loss. However, it is unclear how and to what extent these findings are related to the inflammatory response.
- **Eicosanoids** derived from PUFAs play a part in inflammation, and those from the n-6 PUFAs are *pro-inflammatory*. Their synthesis is competitively inhibited by EPA and DHA present in oily fish, and the eicosanoids produced by the n-3 PUFAs may be *anti-inflammatory*.
- Additional effects of n-3 PUFAs may include increased plaque stability and altered cytokine production. However, at present, it remains unclear how the n-3 PUFAs exert the documented protective effect in CVD.

Haemostatic factors

The balance between *clotting tendency* and *fibrinolysis* determines the risk of thrombus formation. A large number of physiological factors have a role in these processes:
- **Obesity** has been associated with a raised concentration of fibrinogen and other markers of prothrombotic tendency. Weight loss and physical activity have a positive effect on these markers. Some of the contributors to a high energy intake may also affect thrombotic state; for example, heavy alcohol consumption and a high-fat diet both reduce fibrinolytic activity. However, moderate alcohol intakes may reduce fibrinogen concentration.
- Fibrinolytic activity is also improved by diets that promote weight loss, such as low-fat and high-fibre diets.
- **Fish oils**, providing n-3 PUFAs, attenuate the production of thromboxane $A_2$, and so suppress activation of platelets.

Other dietary factors impacting lipids

Other foods and nutrients that have been associated with effects on blood lipids include:
- **Soya**: Isoflavones are able to reduce plasma cholesterol. A reduction of 0.23 mmol/L with an intake of 25 g soya protein/day has been reported.
- **Dietary fibre**: Soluble fibre has been reported to reduce total cholesterol by 0.045 mmol/L for each gram of fibre. Population studies suggest that lower rates of CHD are associated with larger intakes of dietary fibre.
- **Alcohol**: Moderate intakes of alcohol (1–2 units per day) have been shown to reduce CHD in men (above 40 years) and postmenopausal women. Levels of HDLs are increased, but greater consumption increases triacylglycerol and CHD risk.
- **Plant stanols and sterols**: These reduce the absorption of dietary cholesterol and may also increase the activity of the LDL receptor and have a clear effect on reducing plasma cholesterol levels, especially in the LDL fraction.

Key dietary aspects

- Moderate total fat intake.
- Replace the saturated fats with polyunsaturated fats or preferably monounsaturated fats.
- Increase intake of n-3 polyunsaturated fats, preferably from oily fish.
- Consume at least five portions of fruit and vegetables per day.
- Eat wholegrain products to increase dietary fibre intake and provide additional micronutrients.
- If alcohol is included, consume in moderate amounts only.
- Maintain healthy body weight and remain physically active.

Summary

Taking all the stages of the pathological process individually enables a detailed breakdown of the associated dietary factors to be considered. However, many factors have effects across several components of the process, and these form the basis of dietary advice for prevention of CVD.