Nutrition at a Glance
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Contents

Part 1 Nutritional principles
1 Diet, health and disease 6
2 Methods of studying nutrition: nutritional epidemiology 8
3 Nutritional assessment of individuals 10
4 Inadequate nutritional intakes: causes 12
5 Inadequate nutritional intakes: consequences 14
6 Excessive or unbalanced nutritional intakes 16
7 Definitions of an adequate diet 18
8 Creating an adequate diet 20
9 Food choice: internal and external factors 22
10 Food choice: the food environment 24

Part 2 Components of a balanced diet: the nutrients and dietary factors
11 Introduction to the nutrients 26
12 Carbohydrates in the diet 28
13 Carbohydrates in the body 30
14 Introduction to fats: types of fatty acids 32
15 Introduction to fats: related compounds and fat digestion 34
16 Fats: utilisation in the body 36
17 Proteins: chemistry and digestion 38
18 Proteins: functions in the body 40
19 Proteins: needs and sources 42
20 Energy intake: food sources 44
21 Energy intake: control 46
22 Energy requirements: measurement 48
23 Energy requirements: components 50
24 Micronutrients and the heart and circulatory system I 52
25 Micronutrients and the heart and circulatory system II 54
26 Micronutrients: role in metabolism 56
27 Micronutrients: protective and defence roles I 58
28 Micronutrients: protective and defence roles II 60
29 Micronutrients: structural role I 62
30 Micronutrients: structural role II 64
31 Alcohol in the diet 66
32 Fluids in the diet 68

Part 3 The role of nutrition in key organs/systems for the supply of nutrients
33 Nutrition and the gastrointestinal tract I 70
34 Nutrition and the gastrointestinal tract II 72
35 Nutrition and the brain I 74
36 Nutrition and the brain II 76
37 Nutrition and the eye 78

Part 4 Physiological and other challenges to meeting nutritional needs
38 Nutrition in pregnancy and lactation 80
39 Nutrition in infants and preschool children 82
40 Nutrition in school-age children and adolescents 84
41 Nutritional problems in infants, children and adolescents 86
42 Nutrition and early origins of adult disease 88
43 Nutrition in older adults 90
44 Nutrition in ethnic minority groups and impact of religion on diet 92
45 Nutrition and sport I 94
46 Nutrition and sport II 96
47 Adverse reactions to food I 98
48 Adverse reactions to food II 100

Part 5 Nutrition-related disease
49 Overweight and obesity: aetiological factors 102
50 Overweight and obesity: consequences for health I 104
51 Overweight and obesity: consequences for health II 106
52 Overweight and obesity: prevention and management 108
53 Overweight and obesity: popular slimming diets 110
54 Underweight and negative energy balance 112
55 Nutrition and cancer I 114
56 Nutrition and cancer II 116
57 Diet and cardiovascular disease: aetiology 118
58 Diet and cardiovascular disease: prevention 120

Part 6 Improving diets
59 Optimising nutrition 122
60 Promoting nutritional health: a public health perspective I 124
61 Promoting nutritional health: a public health perspective II 126
62 Promoting nutritional health: the role of the dietitian 128

Appendix 1 The vitamins: summary of functions and food sources 130
Appendix 2 The minerals: summary of functions and food sources 131
Appendix 3 Department of Health Report on Health and Social Subjects: Dietary reference values for food energy and nutrients for the United Kingdom 132
Glossary 136
Index 139
Diet, health and disease

Aims
(1) To gain a perspective on some of the links between diet, health and disease.
(2) To recognise the complexity of some relationships between diet, health and disease.
(3) To start to recognise the role of nutritional epidemiology in the study of such relationships.

A healthy diet and lifestyle are generally recognised as pre-requisites for health, defined as the promotion of quality of life, or wellness, and the prevention of nutrition-related disease.

Identifying specific components of diet and lifestyle that can ensure health remains a challenge, as the relationships are complex. Scientific approaches, such as nutritional epidemiology, can provide evidence on which advice and policy can be based. Developments parallel advances in scientific methodology, which allow new approaches to be used in nutritional studies.

Historical perspective
Early studies in nutrition originated from observations of deficiency diseases, for which the cure with a single nutrient was eventually discovered. This led the way to the identification of many of the micronutrients. (see Table 1.1). Examples include:

- Scurvy was observed in sailors on long sea voyages and was treated in the eighteenth century with citrus fruits. It was not identified as a vitamin C deficiency until the early twentieth century, when the guinea pig was found to be susceptible to the deficiency.
- Beri-beri, the deficiency of thiamin, was discovered in Java, in humans and birds fed polished rice; it could be cured by feeding the rice bran, which was eventually shown to be rich in the vitamin.
- The association between low levels of iodine in food and drinking water and the swelling of the thyroid gland, known as goitre, was described in the early nineteenth century. However, the key role of water and the swelling of the thyroid gland, known as goitre, was described in the early nineteenth century. However, the key role of iodine in the formation of thyroid hormones was not elucidated until the early part of the twentieth century.
- Iron, folate and vitamin B12 deficiencies are associated with anaemias that have distinct cytological pictures. Although the common feature was anaemia, its origin involved different dietary patterns, and required differential diagnosis and treatments.

- Some relationships proved to involve several factors, e.g. the development of rickets as a result of vitamin D deficiency. Although it can be obtained in the diet, for most people synthesis in the skin on exposure to sunlight is the most important source of the vitamin. Exposure to ‘country air’, out of smoky cities, was believed initially to be the cure. More recently, it has also been shown that hydroxylation of the vitamin takes place in the liver and kidney, to produce the active form, so an association with disease in these organs also causes the deficiency. Additional roles for vitamin D in cellular metabolism have now been described.

More lessons about the link between diet and disease have been learned from instances of toxicity resulting from overconsumption of dietary factors. Classic examples include:

- Toxic effects from excess intake of vitamin A were recorded in polar explorers consuming the liver of polar bears. More recently, excessive intake of vitamin A, often as a supplement, has been shown to cause fetal malformations in early pregnancy, and may cause bone fractures.
- Hypercalcaemia in infants in the early 1950s resulted from excessive intakes of formula milk and cod-liver oil supplements containing large amounts of vitamin D.

- Excessive intakes of alcohol over time are known to cause liver damage, but the exact aetiology of this toxic effect is likely to be multifactorial, involving other dietary changes consequent on alcohol consumption.

Once the link between a nutrient and disease was established, public health measures were introduced to treat the condition.

Simple measures to rectify deficiencies of individual nutrients
- Parboiling of rice before it is milled ensures that some of the thiamin in the husk is transferred into the grain and improves its thiamin content.
- In iodine-deficient areas the addition of iodine to common salt ensures that a frequently used commodity provides the missing nutrient, and reduces the burden of deficiency.
- When formula milk was introduced in the UK for infant feeding, it was fortified with vitamins A and D. The level of vitamin D was initially excessive (see above). Present-day infant milks are carefully formulated to provide nutrients in amounts that match those in human milk.
- Women of child-bearing age who might become pregnant are advised to take a folic acid supplement as a measure to reduce the risk of neural-tube defects (NTD) in the infant. This is not based on traditional deficiency studies but on evidence from trials showing that such supplementation does reduce the risk of NTD. In the USA, grain products are supplemented with folate, and there has been a significant reduction in NTD cases. This measure is now being considered in the UK.

Table 1.1 Examples of nutrition-related disease predominantly associated with single dietary factors.

<table>
<thead>
<tr>
<th>Disease/abnormality</th>
<th>Dietary factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficiency</td>
<td></td>
</tr>
<tr>
<td>Scurvy</td>
<td>Vitamin C</td>
</tr>
<tr>
<td>Beri-beri</td>
<td>Thiamin</td>
</tr>
<tr>
<td>Goitre</td>
<td>Iodine</td>
</tr>
<tr>
<td>Rickets</td>
<td>Vitamin D</td>
</tr>
<tr>
<td>Anaemia</td>
<td>Iron/folate/vitamin B12</td>
</tr>
<tr>
<td>Overconsumption</td>
<td></td>
</tr>
<tr>
<td>Total abnormalities</td>
<td></td>
</tr>
<tr>
<td>Infant hypercalcaemia</td>
<td>Vitamin A</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>Vitamin D</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
</tr>
</tbody>
</table>
Several dietary factors implicated in disease
In some diseases, the role of individual dietary components is difficult to identify. Ongoing research adds further understanding, but also raises more questions. This can be illustrated for cardiovascular disease and cancer (see Box).

Other factors affecting susceptibility to disease
Dietary factors do not operate in isolation, their effects are modified or amplified by fixed or changeable factors, including:
- genetic susceptibility;
- aspects of early life in the uterine environment;
- environmental factors in the individual’s life;
- lifestyle.

Even for a condition, such as overweight, that has an apparently simple cause (excessive energy intake in relation to output), the exact mechanisms involved and the ways to intervene for any one individual are not easy to find.

Examples of more complex conditions, with several dietary factors implicated
Cardiovascular disease
- Early studies showed that the nature of the dietary fat consumed was important, with cholesterol intake and a high intake of saturated fat being contributory to raised plasma cholesterol levels.
- More recently the benefits of monounsaturated fats, such as those consumed in a Mediterranean diet, have been recognised.
- The balance between different types of polyunsaturated fats is now also seen as relevant, including the importance of fish oils.
- Other aspects of the diet are also implicated, including the intake of sources of antioxidants (as marked by fruit and vegetable intake), dietary fibre, alcohol, salt and possibly the type of carbohydrate.

Cancer
- Its study is exacerbated by the long time lapse between exposure to causative factors and the diagnosis of the disease.
- Dietary factors implicated have included fat, meat, alcohol, salt, lack of dietary fibre, low fruit and vegetable intakes, dietary carcinogens and excess energy.
- In addition, cancers at different sites appear to be associated with different dietary factors.

All of these interlinking factors make it very difficult to:
- identify precisely the role of any single dietary component;
- formulate policy to advise on and influence change.

Further, it should be recognised that in the diet–health–disease relationship, different factors may be involved in the initiation of the disease and others in the progression of the disease. Disease prevention may involve yet other factors and these limitations must be taken into account in the formulation of public health advice.

Introduction to nutritional epidemiology
(1) This is the major scientific method for the study of the relationship between exposure to particular dietary factors and the outcome in terms of causation or prevention of disease; it investigates the strength of such relationships.
(2) It cannot, however, establish a definitive cause for an outcome.
(3) A number of established standards (see Box) must be fulfilled before any conclusions about causality can be drawn. The absence of any one of these standards does not necessarily preclude a relationship between exposure and outcome, but may imply that further information is needed.
(4) Epidemiological evidence is usually collected from groups of people when it is impossible or impractical to collect experimental evidence, but once a causal relationship has been identified, experimental studies may be developed to test this.

Key standards that can suggest the existence of a causal relationship between dietary factor(s) and health/disease outcome
- There is a dose–response relationship between exposure and outcome.
- The relationship is biologically plausible.
- The response is consistent across different populations.
- Exposure to the dietary factor precedes the outcome.
- The relationship between exposure and outcome is strong.
- Bias and/or confounding of both exposure and/or outcome by alternative factors is absent.
- Study design and methods are appropriate.

In summary, the relationship between diet and disease may be simple where individual nutrients are involved, and can be readily replaced to treat a deficiency disease. For the majority of nutrition-related diseases seen in populations today, the relationship with diet is complex. This is because diets are complex and difficult to measure accurately. In addition, variations in individual susceptibility are increasingly recognised. More detailed and accurate techniques are being used in epidemiological studies to meet the challenge.
2 Methods of studying nutrition: nutritional epidemiology

Aims
(1) To introduce nutritional epidemiology methods and their application.
(2) To consider advantages and disadvantages of available methods.

The role of nutrition in health is based on information about food intakes and about health indicators (exposure and outcome). This is addressed by nutritional epidemiology techniques in groups of people.

Study design
- Design is dictated by the research question to be asked (Table 2.1).
- Appropriate measurements must be used.
- Must compare like with like (internal validity) and ensure that any findings can be inferred back to the population from which the sample studied was drawn (external validity).

Measurements relevant to nutritional epidemiology
Investigations of the relationship between exposure and outcome cannot usually measure the exact exposure, as this will have occurred at an unspecified point or period of time. Therefore indirect markers, which can give an indication of the exposure, are used. Some of the same markers may also be indicative of outcome. Those most commonly used in nutritional studies are:
- food intake;
- biomarkers/clinical indicators;
- anthropometry.

Further, as diet-related behaviour does not exist in isolation, but is affected by socio-demographic and cultural factors, these may also need to be included in studies.

Assessment of food intake
This can be performed at group or individual level, depending on the nature of the study (Table 2.2).

Individual food intake measurement is the most common tool used in nutritional epidemiology (Table 2.3).

Food intake measures can be flawed: under-reporting can occur in all methods, as subjects fail to record, or alter their eating habits. This may account for up to 25% of intake; fat- and carbohydrate-rich foods are most likely to be under-reported. If energy intake falls below 1.2 the calculated BMR for an individual, it is highly likely to be under-reported.

Biomarkers
These include assessment of levels of nutrients or their derived products, such as enzymes (Table 2.4). Biomarkers may be influenced by hormone levels and activity of transport proteins, making it difficult to extrapolate to nutrient intake for some nutrients. Individual inherited differences in genes (polymorphisms) affect responses of markers both to nutrients and to lifestyle factors. New biomarkers related to molecular-level activities of nutrients or harmful agents are being developed.

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>Examples of study designs used in nutritional epidemiology.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td>Key features</td>
</tr>
<tr>
<td>Ecological study</td>
<td>Compare different areas, possibly over time</td>
</tr>
<tr>
<td></td>
<td>Measure exposure to a factor (nutrient intake), against the prevalence rate of the disease (outcome)</td>
</tr>
<tr>
<td>Cross-sectional design</td>
<td>Measure exposure and outcome at a point in time, in a population</td>
</tr>
<tr>
<td>(prevalence studies)</td>
<td>If repeated, can be used to monitor trends</td>
</tr>
<tr>
<td>Cohort study</td>
<td>Sample (cohort) studied at baseline and followed up to monitor new disease in those exposed/not exposed to the factor studied</td>
</tr>
<tr>
<td></td>
<td>Relative risk (RR) is the incidence of disease in the exposed group compared to the unexposed group</td>
</tr>
<tr>
<td></td>
<td>Can be used to study multiple outcomes and complex dietary patterns</td>
</tr>
<tr>
<td>Case-control studies</td>
<td>Data about exposure to the factor(s) being studied collected from people who have the outcome/disease and a matched sample without the disease</td>
</tr>
<tr>
<td>Clinical trials</td>
<td>Considered to be the ‘gold standard’ method</td>
</tr>
<tr>
<td>randomised controlled trials</td>
<td>(RCTs)</td>
</tr>
<tr>
<td>Community trials</td>
<td>Intervention is made within a community, e.g. town, workplace, school</td>
</tr>
</tbody>
</table>
Clinical indicators provide valuable information about the state of health of the study population. Measures used can include:

- blood pressure;
- plasma cholesterol levels;
- presence and function of teeth;
- presence of disease (infection, diabetes, cancer, bowel diseases);
- muscle function, grip strength.

### Anthropometry

Specific measurements of body size and changes in proportions are important indicators of nutritional state. These include:

- Weight and height – used to calculate body mass index in adults (BMI), and as indicators of wasting and stunting in children.
- Circumferences: mid-arm muscle (MAMC) can indicate undernutrition in children; waist:hip ratio (WHR) is an indicator of central adiposity in adults.
- Skinfold thickness – is a measure of subcutaneous adipose tissue, and if measured at the appropriate sites (mid-biceps, mid-triceps, subscapular and suprailiac) can be used to calculate percent body fat.

Almost all aspects of the study of nutrition have potential drawbacks. Some can be eliminated with careful planning and design of studies, and where possible with repeated measures. In attempting to link exposure to a causative (or preventive) factor, and a health (or disease) outcome, the multifactorial nature of relationships needs to be considered to prevent inappropriate conclusions being made.
Nutritional assessment of individuals

**Aims**
(1) To examine ways of obtaining information about the nutritional status of individuals.
(2) To explore the uses and limitations of such information.

The techniques used in nutritional epidemiology (see Chapter 2) are also suitable for assessment of individuals.

**Food intakes**
In assessing individual food intakes, a compromise often occurs between an accurate assessment and one that represents normal food intakes (Table 3.1).

Nutrient intakes are calculated using food composition tables. Estimation of portion sizes and allowance for wastage also needs to be considered.

**Anthropometry**
**Height and weight** are the most commonly used measures, as the equipment needed is relatively simple and widely available. Weighing scales, stadiometers and any tapes for surrogate height measures should be regularly calibrated.

In children, growth charts are available (e.g. UK Child Growth Foundation, WHO) to plot serial measurement of height/length, weight and also head circumference during growth and development. Growth should follow a centile, and substantial drift from this needs to be investigated.

Assessment of undernutrition, and its treatment, can be made on the basis of weight and height measurements (Table 3.2).

In adults, height and weight are combined as Body Mass Index (BMI), calculated by dividing weight (kilograms) by height² (metres).

BMI is used in international comparisons, but it does have shortcomings:
• the association of excessive weight with fat deposits may not apply in muscular individuals;
• in older subjects, loss of height may give spurious results.

WHO has defined a number of BMI ranges; these represent risk of associated disease (Table 3.3). (For some population groups, such as South Asians, health risks may increase at lower levels of BMI, with a desirable range from 19–23, and obesity starting at >27.5.)

### Table 3.1
<table>
<thead>
<tr>
<th>Method of assessment</th>
<th>Information provided</th>
<th>Uses/limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duplicate diets</td>
<td>Accurate measure of what has been eaten</td>
<td>May not be typical diet of subject, used in metabolic studies. Expensive</td>
</tr>
<tr>
<td>Food record (weighed, household measures, food photographs, food models)</td>
<td>Current food intake in ‘free living’ individual; portion size information varies with method</td>
<td>Gave an indication of nutrient intake</td>
</tr>
<tr>
<td>Food frequency questionnaire</td>
<td>Typical food intake over a period of time; may be focused on particular foods of interest relevant to the study</td>
<td>Affected by seasonality</td>
</tr>
<tr>
<td>24-hour recall and diet history</td>
<td>Recent food intake or typical food intake pattern, obtained by direct questioning</td>
<td>Can establish dietary pattern, especially for food groups present/absent from the diet</td>
</tr>
</tbody>
</table>

### Table 3.2
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Children</em></td>
<td></td>
</tr>
<tr>
<td>Weight for age, &lt;2 standard deviations (SD) (or Z scores) below reference</td>
<td>Underweight: insufficient food intake currently</td>
</tr>
<tr>
<td>Height for age, &lt;2 SD (or Z scores) below reference</td>
<td>Stunting: chronic undernutrition, affecting linear growth</td>
</tr>
<tr>
<td>Weight for height, &lt;2 SD (or Z scores) below reference</td>
<td>Wasting: acute growth disturbance, change in body proportions</td>
</tr>
<tr>
<td><em>Adults</em></td>
<td></td>
</tr>
<tr>
<td>BMI &lt;18.5 kg/m²</td>
<td>Chronic energy deficiency due to poor food intake or chronic disease</td>
</tr>
<tr>
<td>BMI &lt;17.0 kg/m²</td>
<td>Reduced physical capacity likely to increase susceptibility to illness</td>
</tr>
</tbody>
</table>

Problems in measuring weight and height may arise in individuals who are:
- Bed or chair bound
- Severely overweight
- Unable to stand up vertically (or lie flat)

Surrogate measures of height are available:
Knee height/lower leg length, ulnar length or demispan may be used with appropriate equations (although results for height may vary between these measures, they are adequate for BMI assessment).
Nutritional assessment of individuals

Nutritional principles

Circumferences
Waist circumference, midway between the lower rib margin and the iliac crest, taken at the end of expiration, reflects visceral adiposity, and is sensitive to weight changes. Based on waist circumference, ‘action levels’ have been defined, related to level of risk to health (Table 3.4).

If hip circumference is also measured at the largest part of the buttocks, the ratio of waist to hip circumference (WHR) can indicate the distribution of body fat between central and peripheral regions. A ratio above 0.8 in women and 0.9 in men is taken as a measure of abdominal obesity; increasing values indicate higher levels of risk.

Mid-arm circumference (MAC) is a measure of the circumference at the midpoint of the upper arm, which is used, together with measurement of subcutaneous body fat (by skinfold thickness at the mid-triceps), to assess muscle circumference (mid-arm muscle circumference MAMC), and therefore indicate any wasting.

Body composition
The body is traditionally viewed as being made up of several compartments:
• fat mass;
• fat-free mass (protein and mineral);
• total body water.

Skinfold calipers are used at specific sites in the body (mid-biceps, mid-triceps, subscapular and suprailliac) to assess the thickness of the subcutaneous layer of fat, which represents the major proportion of total body fat. By inputting the measurements into a prediction equation, the percentage of body fat can be calculated.

Table 3.3 Classification of body fatness, based on BMI (WHO).

<table>
<thead>
<tr>
<th>Category</th>
<th>BMI range (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>18.5–24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25–29.9</td>
</tr>
<tr>
<td>Obesity – class 1</td>
<td>30–34.9</td>
</tr>
<tr>
<td>Obesity – class 2</td>
<td>35–39.9</td>
</tr>
<tr>
<td>Obesity – class 3</td>
<td>&gt;40.0</td>
</tr>
</tbody>
</table>

Other methods for measuring body composition

Densitometry – subjects are weighed in air and immersed in water; appropriate equations are used to calculate body fat from the difference in weights. Air displacement plethysmography removes the need to be submerged in water.

Imaging techniques – use computed tomography or magnetic resonance imaging, to visualise discrete deposits of body fat, especially in the visceral region. Dual energy X-ray examination (DEXA) can also be used to predict visceral fat deposits.

Bioelectrical impedance analysis (BIA) – measures the resistance (or impedance) to a small electric current passed through electrodes attached to the hands and feet. Resistance is related to the level of total body water and fat-free mass, which is inversely related to fat mass. Although widely used, the technique is subject to error related to food intake, level of hydration and environmental temperature.

Dilution techniques – body water can be estimated from the concentration of radioactive isotopes injected into the body.

Urinary excretion of metabolites – such as creatinine and nitrogen indicates turnover of body protein and is an indicator of the fat-free mass.

Clinical indicators and biomarkers
A wide range of physical, biochemical and haematological assessments can be used in individuals. In the clinical setting, a number of these are part of the screening and assessment of individuals for nutritional support.

Screening is generally performed with a quick and simple tool, which can be used by a trained member of the nursing or other staff, either in the hospital or other settings. Key points assessed are generally:
• Current body mass index.
• Weight loss (unintentional changes over the recent past).
• Ability to consume food – likelihood of future weight loss.

The Malnutrition Universal Screening Tool (MUST) is a validated tool, widely used in the UK for nutritional screening. On the basis of the score, a patient may be ranked from low to high risk, and can then be referred for a more in-depth nutritional assessment, by a diettian or a member of the nutrition support team.

Summary
Nutritional assessment of individuals includes a number of approaches. Describing and assessing the nutritional intake can indicate where potential problems may exist and what intervention may be needed.
Aims
(1) To consider how environmental factors may contribute to inadequate intakes.
(2) To recognise the extent of the problem of inadequate nutrition.

Inadequate intakes of specific nutrients and excessive or unbalanced intakes can both result in ill health (morbidity) and possibly death (mortality). The transition between these intake levels is difficult to define, so that nutritional adequacy is best viewed as a spectrum, rather than having fixed boundaries (Figure 4.1).

Causes of inadequate nutrition and associated disease
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 hunger (chronic or seasonal), nutrient deficiencies or periods of starvation/famine.

Contributory factors
Disease prevalence is affected only in part by advances in medical practice and treatment. There are many environmental forces that have a much greater impact, as they affect all aspects of people’s lives. Some examples are given in Table 4.1.

What actual impact these forces have on any single individual will ultimately be determined by the personal choices they make (or are able to make) as well as their individual genetic susceptibility to the effects of the environmental factors.

This individual level of response means that 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 so that inadequate energy intakes are likely to be accompanied by low intakes of other nutrients.

In some diets, nutrients may appear to be present, but are unavailable as a result of:
• binding to other components of the food (inactive form in the
Inadequate nutritional intakes: causes

Nutritional principles

13

food, inactivated by food preparation methods, presence of phytate, dietary fibre); • inhibition/promotion by other dietary factors eaten concurrently (e.g. factors affecting pH in the intestine); • competition by parasitic infestation within the gut; • poor utilisation, e.g. lack of carriers for absorption or transport in the blood, due to malnutrition; • treatment with drugs preventing utilization.

Magnitude of the problem

It is difficult to obtain accurate information about the extent of undernutrition, because data are not collected routinely or are affected by sudden crises (war, environmental disasters) and the growing burden of disease such as HIV, AIDS and tuberculosis (TB) contributing to undernutrition.

Despite a theoretically adequate global food supply, the Food and Agriculture Organization (FAO) of the United Nations estimates that there are approximately 800 million undernourished people in the world, with the majority of these in the developing countries of the world, but also some 11 million in the developed countries. There have been reductions in the overall numbers in the last 20 years, but these vary between countries, with greatest progress in South America and parts of South-East Asia, and least progress in Africa.

In developed countries, inadequate intakes may be found in groups including:

• large families on low incomes;
• marginalised groups in society (e.g. minority ethnic groups, refugees, asylum seekers);
• the homeless;
• people with addictions (e.g. to drugs, alcohol);
• those in need of care who do not receive it (e.g. people with disabilities).

The consequences of inadequate nutrition will vary, and are discussed in Chapter 5.

Table 4.1 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 and dietary patterns in communities</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, transport (food supplies, access to markets)</td>
</tr>
<tr>
<td>Socioeconomic status of groups within population</td>
<td>Access (physical and financial) to safe food of suitable nutritional quality</td>
</tr>
<tr>
<td>Health-care provision</td>
<td>Impact of status on living environment</td>
</tr>
<tr>
<td>Clean water and sanitation</td>
<td>Access to appropriate health care at all life stages (e.g. immunisation, antenatal care, information on infant/child feeding practices, early recognition of disease)</td>
</tr>
<tr>
<td>Education</td>
<td>Less infectious diseases and environmental contamination; reduced nutritional needs to fight infections</td>
</tr>
<tr>
<td>Status of women</td>
<td>Awareness of the importance of diet and health care, lifestyle habits</td>
</tr>
<tr>
<td></td>
<td>Better food production techniques by farmers</td>
</tr>
<tr>
<td></td>
<td>Women generally integrate health measures within a family, higher status allows women to be involved in decision-making</td>
</tr>
</tbody>
</table>