NEAL COOK
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ESSENTIALS OF PATHOPHYSIOLOGY FOR NURSING PRACTICE

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1
VARIATION AND DISEASE

Understand

Chapter videos

Viewing the videos will help you to grasp some of the issues surrounding the care of patients with different diseases.

The videos can be accessed by **scanning the QR code** with your smartphone camera or via **https://study.sagepub.com/essentialpatho2e**.

ACUTE VS CHRONIC (4:13)

CHRONIC DISEASES (2:40)

Learning outcomes

When you have finished studying this chapter you will be able to:

1. Discuss causes of biological and behavioural variation in health and disease.
2. Differentiate between acute, sub-acute, chronic and acute on chronic disease conditions.
3. Identify a range of different causes of disease.
4. Explain factors influencing disease presentation.
5. Understand the importance of diagnosis and identify how signs, symptoms and a range of haematological, biochemical and radiological tests facilitate diagnosis.

INTRODUCTION

When we consider people with the same medical condition, they rarely exhibit exactly the same signs and symptoms at the same stage of their disorder; each journey through illness is largely unique in how it manifests and progresses. This chapter examines how and why individuals differ in health and **disease**. Disease patterns (i.e. **acute**, **sub-acute** and **chronic**), causes and diagnosis of disease are also reviewed.

This chapter builds on the study of anatomy and physiology (e.g. Cook et al., 2021) and aims to develop your understanding of disease through the examination of a number of different factors that influence the development, presentation and progress of ill-health. The focus on person-centred nursing (McCormack and McCance, 2021) throughout this book means that the variation between individuals and how this influences disease must be taken into account in order that we can individualise the provision of care. From your previous and varied areas of study, you will understand how people can differ both biologically and behaviourally, and that these can influence the presentation of disease and how individuals respond.

Within this chapter the categories and causes of disease will be examined. We will discuss how signs, symptoms and a range of haematological, biochemical and radiological tests are used to achieve a diagnosis and guide treatment.

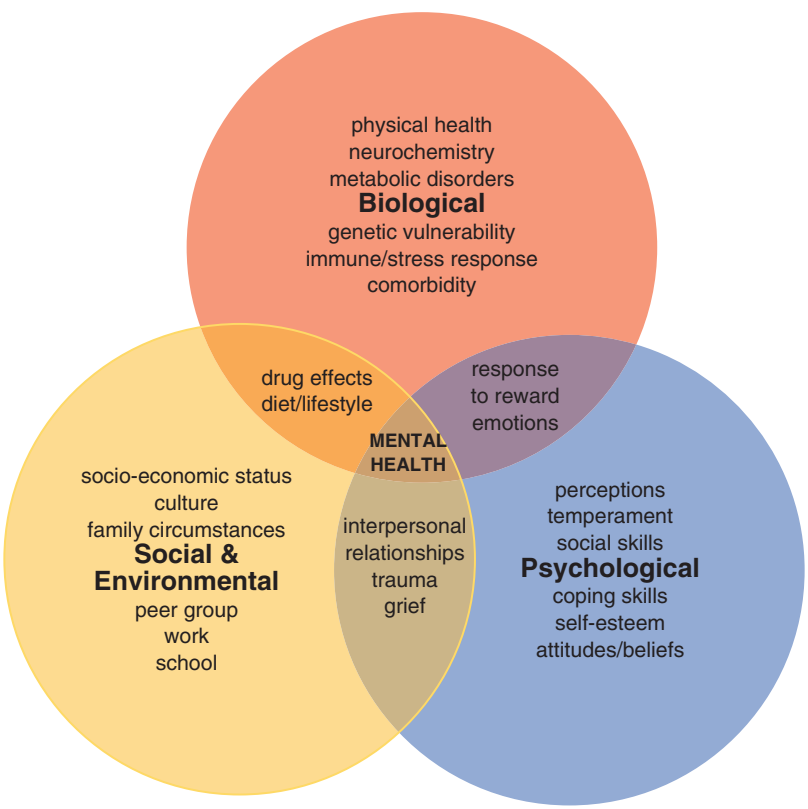

Figure 1.1 Biopsychosocial model of health and mental wellbeing

BIOPSYCHOSOCIAL MODEL OF HEALTH AND MENTAL WELLBEING

As we begin to explore the variation in disease, we must recognise the different influences and contextual factors which play a significant role in how an individual adapts to difficulties they are experiencing or how these challenges impact their quality of life. In 1977, George Engel proposed an alternative approach to the traditional medical model, instead arguing that how an individual experiences a condition, and their attitude towards it, had a significant influence on their health. Engel's (1977) (Figure 1.1) biopsychosocial model of health presented a dynamic interplay between the biological (Chapter 4), social (Chapter 2) and psychological (Chapter 5) factors leading to disease and the variations seen among different patient groups. While widely acknowledged, this model has been the subject of significant critique for its limitations in capturing the full range of human experience and adversity (Bolton and Gillett, 2019). However, the interconnection of the core components provides a vital foundation in which to understand why there are variations in health and what individuals are most vulnerable to them across the life span. Only through this perspective can we truly understand the individualised nature of pathophysiology and the holistic approach to treatment required.

Person-centred context

The Bodie family

Think back to the Bodie family introduced at the start of the book and you will quickly see that there are a number of issues in relation to health that are relevant to this chapter. In general, as a family they are well adapted to any variations in their health and have learned to live fulfilling lives in spite of any illness or disorder. However, there are a number of issues which individuals have to cope with in order to achieve this balance.

Several members of the family have chronic physical disorders which they manage successfully. Following a **myocardial infarction** (heart attack), Maud was diagnosed with **heart failure**, now under good control. She also has **hypothyroidism**, which is successfully managed with medication. Richard has type 2 **diabetes mellitus**, Derek has **asthma** and Margaret has hay fever. However, all of them are managing their conditions effectively.

Richard and Matthew have both suffered from mental health problems. Richard had an acute **stress** response in the past, which was treated effectively with cognitive behavioural therapy. Matthew has had **depression** for 15 years (i.e. a chronic condition), although it is being managed successfully with medication and support from the community mental health team.

Within this family, several of them have undertaken approaches to maintain their health or prevent disease. For example, Hannah and Richard Jones eat a diet containing plenty of wholemeal bread and at least five portions a day of fruit and vegetables. Hannah smoked in her early 20s but gave up a number of years ago.

Still considering prevention, they ensure that they have appropriate **immunisations**: early in life for Danielle (the youngest member of the family); before holidays abroad as appropriate; annually against flu for the two older people and Derek who, as an asthmatic, is at increased risk of respiratory infections.

HUMAN VARIATION

Individuals vary in the ways in which they behave, develop, function and respond to their environment. All of these can influence health, the development of disease and how they respond. There are a number of terms used in describing health status and they need to be clearly understood, as follows:

- *Health*: the WHO (1948) definition is 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'.
- *Disease*: 'any impairment of normal physiological function affecting all or part of an organism, especially a specific pathological change caused by infection, stress, etc., producing characteristic symptoms; illness or sickness in general' (Collins English Dictionary, 2012).
- *Illness*: 'poor health resulting from disease of body or mind; sickness' (American Heritage, 2016).
- *Disability*: an umbrella term, covering impairments, activity limitations and participation restrictions. An impairment is a problem in body function or structure, an activity limitation is a difficulty encountered by an individual in executing a task or an action, while a participation restriction is a problem experienced by an individual in involvement in life situations (WHO, 2018).

Altered health status can be considered as a disturbance from normal. But we need to ask *what is normal?* The use of the term 'normal' is controversial in health care and largely relates to factors being within healthy, homeostatic parameters. Various aspects of variation are considered and help to clarify what is 'normal'.

Physical variation

Physiologically, normality and abnormality are defined in relation to certain limits. Measurements of anatomical, physiological and biochemical characteristics are interpreted by comparison with standards; standard norms (i.e. the range of normal) are obtained by measuring the specific characteristic in large numbers of readily available subjects, who are representative of the population, if possible. However, it is important to take into account that variation in such measurements can occur between ages and ethnic background. Some results which indicate disorder in some groups may be within normal limits for others and, in judging the implication of such results, knowledge and clinical expertise must be applied.

Variation can occur in all aspects of bodily makeup, anatomy, physiology, biochemistry, and growth and development. In essence, such variation is determined by nature (i.e. genetic composition) or nurture (i.e. environmental factors) but is largely a combination of both. The factors involved can be related to such circumstances as: age, gender, ethnic background, or environmental conditions, including **nutrition**, during development or later in life. A number of examples of such variations are presented in Table 1.1 based on work by Overfield (2017), which is a useful text with wide coverage of human variation.

Susceptibility to disease is another issue that varies across individuals and will be indicated as relevant in this book.

Behavioural variation

We have considered a range of factors that cause variation in the biological parameters shown in Table 1.1 and which need to be taken into account in understanding the presentation of disease. However, human

behaviour is also important in causation of and response to disease and merits some consideration here: it is based on a mix of nature and nurture.

Behaviours associated with lifestyle, and often with an element of choice, can play an important role in the development of disease. Many diseases, particularly chronic ones, are a result of lifestyle factors, including diet, exercise, smoking, and use of drugs or alcohol. While some of these occur through choice, some do not; for example, poverty can limit the ability to purchase adequate healthy food. These issues receive further attention in Chapter 2 (Health and Disease in Society) which considers **epidemiology** and health promotion.

Management of stressful events is also important in promoting or damaging health. The way in which individuals respond to illness can influence their physiological functioning, as discussed in the section on Stress later in this chapter.

Table 1.1 Variation in biological characteristics

Characteristic	Variation
ANATOMICAL VARIATION	
Height/weight	1. Less than genetically programmed height: inadequate nutrition during period of growth, or insufficient production of hormones affecting growth
	2. Long limbs and digits: occurs when growing up in a hot climate (enhances heat loss); also in **Marfan syndrome** – a genetic disorder of **connective tissue**
Chest size	Enlarged thorax: growing up at high altitudes; low oxygen levels stimulate growth of enhanced chest capacity for respiration
Bones	Density increased and muscle attachments on bone are larger when exposed to strong forces (e.g. from heavy work)
	Bone density may be reduced when inadequate **vitamin D** production occurs due to limited exposure to sun
PHYSIOLOGICAL VARIATION	
Adult lactose tolerance (Deng et al., 2015)	Varies with areas of historic cattle domestication: 90% N. European; ↓ 50% in Spain, Italy, pastoralist Arabian populations; low in Asia and most of Africa.
	Intolerance causes bloating, flatulence and cramps
Heat tolerance (Daanen and van Marken Lichtenbelt, 2016; Foster and Collard, 2013)	1. Body size increases as temperature decreases. Bodies of people living in colder climates tend to be larger than those in warmer climates, and more suited to the cold. This applies with considerable differences in latitude and temperature between groups
	2. Children and older people tolerate heat less well
BIOCHEMICAL VARIATION	
Malaria susceptibility	Several variations in the structure of **haemoglobin** or of red blood cell enzymes in heterozygotes (i.e. only one gene carried) protect individuals against malaria to some extent. Examples of such conditions include:
	Sickle cell **anaemia**, thalassaemia, glucose-6-phosphate dehydrogenase (G6PD) deficiency, Duffy blood group
Drug metabolism	1. Atypical form of pseudocholinesterase (enzyme which degrades succinylcholine – a muscle relaxant used in **surgery**) – results in prolonged paralysis and an inability to breathe
	2. Slow or fast inactivation of isoniazid (used in treatment of TB) will alter level of drug in body and efficacy of treatment and susceptibility to side-effects

(Continued)

Table 1.1 (Continued)

Characteristic	Variation
VARIATION IN GROWTH AND DEVELOPMENT	
Pelvic size and fetal maturity	African women: smaller pelvis and smaller baby than Caucasian (white) women, but babies are more mature for same weight than Caucasian babies
Growth curves	Growth curves are similar shape for different racial groups, but growth spurts in Asian children occur later than in Caucasian children

Source: Adapted from Overfield, 2017

DISEASE PRESENTATIONS

Disease is a state of disordered functioning and in this book we are focused mainly on disordered physiological function as defined by the medical practitioner. However, understanding of physiological disturbances resulting in mental ill-health is increasing and will receive some attention. Differing from this is the illness suffered by the person affected: this consists of the subjective experience of their symptoms.

There are three broad groups of disease presentations used in medicine: acute, sub-acute and chronic, with differing implications for the individual concerned, for their family and for the relevant health care team. The following sections clarify these different groups of conditions.

Acute

An *acute illness* is one in which signs and symptoms develop suddenly; the condition is usually severe and lasts for a relatively short period of time or becomes sub-acute or chronic if it persists but becomes controlled. It is important to differentiate acute from severe as the terms are sometimes, but incorrectly, used interchangeably. An acute condition can be minor, such as a cut finger, or severe such as a myocardial infarction or fractured femur. In other words, the severity of the condition does not determine whether it is acute, sub-acute or chronic. An example of an acute condition is acute urinary tract infection, which usually recovers fairly quickly with antibiotic therapy. Repeated such infections can result in renal damage and chronic **renal failure**.

In most acute disorders, the person affected will return to their normal health and activity, although some will progress to a chronic state of disease or may die. Table 1.2 gives examples of some acute conditions.

Table 1.2 Examples of acute conditions

Acute myocardial infarction (heart attack)
Acute **bronchitis**
Acute **renal failure**
Acute **hepatitis**
Trauma

When severe, acute conditions often have considerable emotional implications for the individual concerned and for their family as they often require adaptation or lead to a major change in their lives. Independence may be reduced, they may fear further health complications and have a reduced ability to participate in enjoyable activities. While most people adjust over time, care and support are usually necessary to achieve such an adaptation.

Apply

Long-term implications of acute conditions in families

The effect of an acute condition occurring in a close relative can be considerable, as Jack Garcia demonstrates. Jack, Thomas Bodie's partner, undertakes monthly testicular self-examination. His father has a history of testicular cancer and Jack wants to make sure that he identifies it early and gets immediate treatment if it develops. In this respect his health behaviour is healthy but underpinned by caution. Jack is aware of the potential for the condition to occur, causing him and his partner some anxiety. His behaviour also acts as an example for the Bodie family of the importance of regular checking for such acute conditions and the importance of support with them.

Chronic

A chronic condition is one that persists over an extended period of time, described in terms of months and years rather than days and weeks, and usually longer than three months. A considerable number of organs or systems of the body can be affected (Table 1.3).

Table 1.3 Examples of chronic conditions

Physiological conditions	**Hypertension** (cardiovascular system)
	Chronic bronchitis (respiratory system)
	Chronic renal failure (kidneys)
	Chronic hepatitis (liver)
	Multiple sclerosis (nervous system)
	Diabetes mellitus (endocrine system – glucose regulation)
	Rheumatoid arthritis (joints)
	Epilepsy (brain)
	Osteoporosis (bones)
	Ulcerative colitis (large intestine)
Psychological conditions	Alzheimer's disease
	Bipolar disorder

Sometimes the condition is progressive, resulting in an increasing loss of independence and ability over time, for example, in chronic bronchitis. In some conditions, the disorder may plateau, e.g. hypertension can be well controlled with medication. However, in many progressive disorders the deterioration will progress and eventually result in permanent disability or death, e.g. in multiple sclerosis. However, the symptoms can often be kept under control with medication and a healthy lifestyle, thus extending the person's health-related quality of life through managing the condition, such as osteoporosis. This sometimes results in slowing its progression, and may result in a cure.

Some chronic conditions are largely related to health behaviours (see below) such as smoking or a lack of exercise. According to WHO/Europe (2016) non-communicable chronic diseases are the greatest cause of **morbidity** and mortality in the European Region, an example of a highly developed part of the world with highly developed health services. In this region, the major chronic conditions of **cardiovascular disease**, diabetes, respiratory disease, **cancer** and mental health disorders result in an estimated 86% of the deaths and 77% of the disease incidence.

There are also some chronic conditions associated with infections. For example, human immunodeficiency virus (HIV) and **acquired immune deficiency syndrome (AIDS)** are an example of an infective chronic condition caused by a **virus**. Less developed parts of the world have much higher incidences of infective chronic disorders than advanced countries. For example, South Africa has the biggest **epidemic** of HIV/AIDS, with 19.2% of the population infected and with 48% of the adult population receiving antiretroviral medications (AVERT, 2016).

Another microbial grouping with an influence on chronic disease is the herpes virus. This is a complex group of viruses which, over time, have been identified as consisting of 97 species, divided into numerous groupings of families, subfamilies and genera. Of these, the most important in human disease is HHV-6, otherwise known as human herpes virus 6, with two main species, HHV-6A and HHV-6B (discussed jointly as HHV-6). Humans acquire this virus early in life, some as early as one month, and the virus can initiate an active infection, often with a high temperature, inflammation of the tympanic membrane, and **malaise** and irritability. It then becomes latent in salivary glands, blood-forming stem cells and others, and remains established within the host for the individual's lifetime. It can become reactivated at intervals to promote spread of the infection. A range of other infections are associated with this virus, including: hepatitis, febrile **convulsions** and **encephalitis**. It has also been found in people with multiple sclerosis, and is associated with various other disorders, e.g. chronic fatigue syndrome, **fibromyalgia**, AIDS, optic neuritis, temporal lobe epilepsy and cancer (Engdahl et al., 2019; Shikova et al., 2020).

An individual or individuals with chronic illness in the family may have a significant effect on the way of life of the family. As those around us in our daily lives are often our first line of support, it is paramount that the impact of illness on all involved is considered so that their health and provision of social support are not adversely affected. Maintaining as healthy a lifestyle as possible, promoting activity and enhancing quality of life are crucial. Health services need to be exactly that – services that promote health and minimise the occurrence of ill-health. Unfortunately, the majority of health services are focused on managing illness after it has occurred rather than on proactively preventing it or slowing its onset and progression.

Apply

Chronic conditions in the Bodie family

In the Bodie family, the grandparents both have chronic health issues but they live active, happy lives. George is on medication to limit his raised **cholesterol** level. Maud has had an acute myocardial infarction (heart attack) which has resolved but she now has heart failure, managed effectively with medication, and also takes thyroid hormones for low thyroid function.

Among the next generation, Richard has type 2 diabetes, while Derek has asthma; both men are managing their conditions well. In the following generation, Margaret has hay fever, again managed effectively when the pollen count is high. However, the similarities in immune response with hay fever, asthma and **eczema** (the atopic triad) mean that she may also develop asthma as she gets older (Huovinen et al., 1999).

Acute on chronic

The term **acute on chronic** describes the situation where someone with a chronic condition has an acute exacerbation of their condition, requiring more intensive treatment.

Apply

Managing risk of acute on chronic attacks

There are a number of chronic conditions in which the individual affected may have an acute episode on top and may need admission to hospital or emergency care to enable them to return to their normal stable condition. For example, it is not uncommon for someone to have to be taken to hospital with an acute attack of asthma – a condition that Derek in the Bodie family suffers from. Although most people with asthma become knowledgeable about their condition, Derek's medical experience gives him an advantage in managing his condition so that, as yet, he has not had an acute on chronic attack. A number of conditions demonstrate this picture of acute on chronic presentation, including chronic bronchitis, liver disease, **chronic kidney disease** and **rheumatoid arthritis**.

Sub-acute

The term 'sub-acute' refers to conditions that fall between acute and chronic in nature. The illness cannot be regarded as acute but more than meets the criteria for chronic. A classic example is when an older person develops a **subdural haematoma** (a type of blood clot on the brain). Often there is a delay in presentation as the impact in the initial stage is not overly symptomatic. However, as the clot begins to break down (from solid into a more liquid state) it increases in mass and signs and symptoms

become more obvious. This can be over a week from the onset and at this stage is referred to as sub-acute subdural haematoma. Table 1.4 identifies a number of sub-acute conditions.

Table 1.4 Examples of sub-acute conditions

Sub-acute thyroiditis
Sub-acute endocarditis
Sub-acute combined degeneration of the cord (vitamin B_{12} deficiency)

CAUSES OF DISEASE (AETIOLOGY)

Diseases can be either **congenital** or acquired:

- Congenital disorders (defect or anomaly) are conditions which are present at birth. They may be genetically determined (e.g. **cystic fibrosis**) or may be due to some other factor in the uterine environment up to the time of birth. An example of this is the abnormalities resulting from thalidomide, given to women in early pregnancy in the late 1950s and early 1960s to treat morning sickness (McBride, 1961).
- Acquired diseases are those that develop after birth, although they may still be due to prenatal influences. One example of this is **Huntington's chorea** (or Huntington's disease) which is genetically determined, so is pre-determined at conception but does not become manifest until much later in life.

Diseases can also be communicable or non-communicable:

- Communicable disorders (also described as infectious or contagious) are caused by microbes transmitted to people from other people, from animals (zoonoses), or from other reservoirs of infection in the environment. They can be spread through the air, through contact with bodily fluids, or through ingesting infected food or fluids.
- Non-communicable disorders are not contracted by communication with others or by infection, but occur as a result of a range of risk factors. Many of these can be limited through interventions that encourage modification of lifestyle and treatment of physiological factors which can result in disease (Chapter 2). A non-communicable disorder can be traumatic in nature or can develop from unhealthy lifestyle factors such as smoking, poor diet, repeated physical stress on the body and chronic stress/anxiety.

A wide range of factors can result in or predispose to disordered function which may lead to disease and we will look at these in outline (Table 1.5). Later chapters which focus on disorders of specific body systems will consider these as relevant.

FACTORS INFLUENCING DISEASE PRESENTATION

In the section above, causes of disease were examined. A number of issues that influence the presentation of disease are considered next.

Table 1.5 Causes of disordered physiological function

Cause		Examples
Trauma	Acute	Head injury leading to brain trauma
	Chronic	Repetitive **strain** injury (e.g. wrist)
Infection		Pneumonia (lungs), pyelonephritis (kidneys), AIDS/HIV
Immune response		Hay fever, anaphylactic shock, autoimmune disorders
Heat or cold		Burns, frostbite
Ionising radiation		Radiation sickness
Poisons		Alcohol – **cirrhosis** of the liver
		Drugs – hepatitis
		Tobacco smoke – carcinoma of the lung
		Chemicals – asbestosis (lungs), bladder cancer
Inadequate nutrient intake		Kwashiorkor (due to protein deficiency)
		Pernicious anaemia (due to inadequate vitamin B_{12} absorption)
		Anorexia nervosa (nutrient intake restricted due to mental illness)
Excessive nutrient intake		Cardiovascular disease
		Diabetes mellitus type 2
		Obesity (risk of diabetes and other diseases)
Lack of oxygen supply to part of body		**Gangrene** (e.g. of foot or leg)
		Stroke
Altered cell division		Carcinoma of epithelial tissues (e.g. lungs)
		Sarcoma of connective tissues (e.g. bone)

Physiological mechanisms in disease

A number of physiological mechanisms can play a role in disease and are discussed here.

Disordered negative feedback

From your knowledge of physiology (Cook et al., 2021, Chapter 1), you should already understand the way in which negative feedback acts to maintain a steady state (i.e. **homeostasis**) in the various physiological parameters. From a biological perspective, disease can be considered as disordered homeostasis. Under normal circumstances any disturbance from the normal results in changes to minimise that disturbance. Thus, the body compensates for and adapts to any disturbances which threaten the steady state and homeostasis is maintained.

In certain diseases, negative feedback fails and deviations from normal persist or extend. Two examples are:

1. In oversecretion of the thyroid gland hormones, the normal feedback mechanisms which inhibit further secretion of the thyroid hormones fail and high levels of hormone secretion continue.
2. In carcinoma, the contact inhibition which controls cell division through negative feedback fails and cell division continues unchecked.

Stress

Stress is both a response and a causative factor in disease. It is how one's body responds to any demand or threat and the causes or effects may be physiological or psychological in nature. It is caused by a wide range of circumstances – physical illness, social factors, psychological or emotional triggers etc. – known as stressors. Under these circumstances the body automatically activates its defences in the fight-or-flight reaction (initiated through the sympathetic nervous system) or the stress response. There are a number of models of stress but the one we are focusing on is that described by Selye (1976) and used by other authors, including Cox (1978). Much of the literature is relatively old but is still relevant and used by many authors.

From a physiological perspective, the stress response is mediated through the **hypothalamus** and links from this to the limbic system, and thus to the cerebral cortex, ensuring that emotional states influence the stress response. It has a short-acting and a longer-acting aspect and occurs through the action of specific hormones. The secretion of many hormones is influenced in stress but the major ones are:

- *short-acting (acute) response*: involves mainly catecholamines (adrenaline and noradrenaline from the adrenal medulla)
- *longer-acting response*: involves **glucocorticoids** (e.g. cortisol, cortisone etc., from the adrenal cortex) as well as other hormones.

The activities in both aspects of the stress response are to prepare the body to cope with any extra demands placed upon it. In moderation, it is an essential adaptive response (an inability to respond effectively may lead to death), but in excess or in prolonged exposure, it can result in changes which contribute to the presentation of disease. Selye (1976) described the stress response in three stages (Figure 1.2): the Alarm Reaction, the Stage of Resistance and the Stage of Exhaustion.

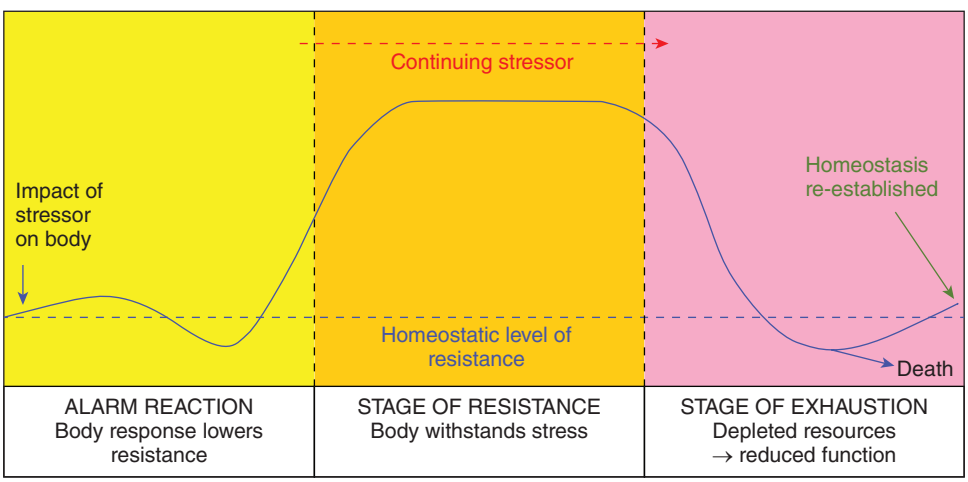

Figure 1.2 The stress response

The acute response to stress overlaps with the Alarm Reaction described by Selye and is also known as the fright, flight or fight response. The physiological changes that occur enable the body to respond rapidly to threat (perceived or actual) (see Table 1.6) and may also occur when people are stressed in illness. Frequent episodes can result in hypertension (high blood pressure) and the changes that occur can result in acute exacerbations in people with chronic conditions.

The changes associated with the longer-lasting stress response are mainly due to increased glucocorticoid secretion and can also have deleterious effects on the person's health (Table 1.6). Some of the changes identified are very important in enabling the body to cope with extra demands. However, if they are prolonged, they can lead to changes which are harmful to the body.

Table 1.6 The alarm reaction /acute stress response

System	Physiological changes	Physical changes	Signs and symptoms
Cardiovascular	Increased cardiac rate and output	Tachycardia, full pulse, raised BP	Palpitations, chest pains, headache
Respiratory	Can lead to low PaO_2 causing vasodilation, fall in BP, low Ca^{2+}	Increased rate and depth of **ventilation** Tetany (muscle spasm)	Dizziness, fainting, panic (in extreme circumstances) Tingling of extremities Tetany (in extreme circumstances)
Gastrointestinal	Reduced blood supply and reduced secretion in gastrointestinal tract (GIT) Decreased or increased motility	Vomiting, diarrhoea, constipation, anorexia or overeating	Dry mouth, indigestion/ dyspepsia (see previous column)
Skin	Contraction of pilomotor muscles Cholinergic sweating Reduced blood supply	Erection of skin hair Sweating Pallor	Clammy palms
Eye	Contraction of radial muscles	Dilated pupils	Blurred vision
Muscle	CNS arousal	Muscle tension, tremor Muscle spasm in severe cases Lack of coordination	Headache, back pain Muscle tension, tremor, twitching Lack of coordination
General	CNS arousal Increased metabolic rate	Insomnia, restlessness Low grade pyrexia	Insomnia, restlessness Fatigue/weakness Feeling hot or cold

Diabetes mellitus has been identified in Table 1.7 as a condition influenced by the stress response. The evidence for stress causing diabetes (type 1 or 2) is mixed: some studies have demonstrated a link between stressful events and the development of type 1 and type 2 diabetes, but other studies have found no such relationship (Wang et al., 2019). However, a number of studies demonstrate a relationship between stress and metabolic control in those with diabetes and the development of complications.

Table 1.7 Main effects of corticosteroids in long-lasting stress response

Body function	Effect of corticosteroids	Physiological changes	Pathological changes
Carbohydrate metabolism	↑ gluconeogenesis ↑ blood glucose level Antagonises **insulin's** peripheral effects	Increased plasma glucose Glycosuria (if renal threshold exceeded)	Diabetes mellitus
Protein metabolism	Protein: ↑ breakdown, ↓ synthesis ↑ amino acid deamination	↑ amino acids in blood ↑ nitrogen content of urine Negative nitrogen balance	Muscle wasting, thinning of skin Loss of hair Depressed immune response
Lipid metabolism	↑ fat breakdown	↑ fatty acid and cholesterol levels ↑ ketone production and **ketonuria**	Adipose tissue redistributed from periphery to head and trunk
Calcium metabolism	Vitamin D metabolites antagonised	↓ calcium absorption from gut ↑ renal **excretion** of calcium	Reduced calcium levels → potential for osteoporosis
Inflammatory response	Lysosomes in cells stabilised **Phagocytosis** suppressed ↓ **collagen** formation ↓ histamine and bradykinin released	Inhibits inflammation ↓ formation of granulation tissue ↓ allergic response	Potential for gastric **ulcer**ation Reduced rate of wound healing
Immune response	↓ immunoglobulin formation ↓ levels of white blood cells **Atrophy** of lymphoid tissue	Decreased white cell count Immunosuppression	Decreased resistance to infection
Fluid and **electrolyte** balance	↑ Na^+ and H_2O resorption in kidneys ↑ K^+ and H^+ excretion	Increased extracellular fluid (ECF)	Potential for **oedema** (fluid in tissues)
Blood	↑ coagulability, ↓ white cells	Reduced blood clotting time	Haemoconcentration, blood clotting
Central nervous system	Emotional changes	Increased rate of learning	Emotional changes with illness

Source: Adapted from Boore, 2000

Stressful experiences could influence lifestyle behaviours which could have a significant impact on the development of type 2 diabetes (Wang et al., 2019). Additionally, the impact of stress differs across genders and may be influenced by the nature of the life event and the age it was experienced (Wang et al., 2019). More recently, Williams et al. (2013) provided evidence that perceived stress predicted abnormal glucose metabolism in women but not in men.

Apply

Stress and diabetes

Within the Bodie family, Richard demonstrates a possible link between stress and diabetes. He was successfully treated by cognitive behavioural therapy (CBT) for stress some time ago and has had type 2 diabetes for the last 5 years. CBT may have focused on stress management, as identified by Lloyd et al. (2005), who described three stages:

- Removing or minimising the source of stress
- Changing the response to stress
- Modifying the longer-term effects of stress.

If this was the focus of treatment, it is likely to have enhanced Richard's management of stress and his diabetes, resulting in better blood glucose control. He is managing his diabetes well, with blood glucose levels remaining within acceptable levels. The diet taken by him and Hannah facilitates diabetes management and her support helps him.

Psychological stress

Many of the physiological mechanisms involved in stress are identified in Tables 1.6 and 1.7 but there are also important psychological mechanisms at play that can lead to behavioural coping strategies which may be extremely varied, and the cause or result of stress. Psychological stress can develop in any situation where there are negative or uncontrollable events that impact an individual's sense of self. This can be caused by the external or internal expectations placed upon an individual and the available resources they have to meet them. Such psychological stress can cause a physiological reaction by stimulating the arousal system within the body. While the demands on the individual exceed their available supportive resources, there can be perceived risk to their identity, raising the potential for mental health difficulties (Bolton and Gillett, 2019). In reactions to stressors, emotional distress can lead to unhealthy behaviours or dangerous lifestyle choices; these can include smoking, drinking alcohol excessively, excessive eating (often of sweet things) to provide comfort, with potentially harmful effects on the body. Other chronic disorders may also be influenced by stress, and stress management is an important aspect of person-centred nursing. Psychological distress can, therefore, be a causative and resultant effect of stressors and must be recognised in the treatment of any condition.

Circadian rhythm is the normal 24-hour rhythm that occurs in many physiological parameters such as body temperature, hormone secretion etc. Disturbed circadian rhythm can also result in a stress response and be indicative of psychological distress.

Activity 1.1: Understand

Circadian rhythm

As you watch this video about circadian rhythms, think about the Bodie family: enforced change in circadian rhythm, such as working night shifts, can result in stress, as already considered. As an airline pilot, this is an important issue for Thomas Bodie, who finds himself working a range of different hours and across time zones. Circadian rhythm is also a factor which may influence the presentation or severity of disease or the efficacy of drug therapy.

(Continued)

The video can be accessed by **scanning the QR code** with your smartphone camera or via **https://study.sagepub.com/essentialpatho2e**.

CIRCADIAN RHYTHM
(11:19 MINS)

Ageing

Variation between individuals increases with ageing as the rate of decline of physiological functions differs. The causes of ageing are still being researched but Wang et al. (2013) have discussed the effects of oxidative stress response due to mitochondrial dysfunction on ageing.

Understand

Reactive oxygen species and ageing

Reactive oxygen species (ROS) are oxygen-containing molecules formed as a by-product of normal oxygen metabolism and which play important roles in cell signalling and homeostasis.

A mild oxidative stress response from the **mitochondria** is important in regulating adaptation and having an anti-ageing function. However, excessive ROS can result in damage to cellular components and initiate **apoptosis** (programmed cell death) through action of the mitochondria (Wang et al., 2013).

An older person's physiology may be affected in various ways. For example, deficiencies in endocrine function can occur in older people, particularly in the hormones associated with the reproductive systems and growth hormone. The endocrine functions essential for life (controlled by the adrenal and thyroid glands) show minimal overall changes with ageing although there are changes in the **hypothalamic-pituitary-adrenal**/thyroid axis (van den Beld et al., 2018).

An older person may have very little reserve capacity for maintaining homeostasis and even a minor event, such as a cold, can initiate a series of physiological disturbances and result in disease. The person may, or may not, achieve a new equilibrium. The physiological changes that occur in ageing will influence the presentation of disease. Table 1.8 indicates some of the changes that occur with normal ageing and the major clinical implications.

Table 1.8 Ageing and its clinical implications

System	Physiological changes	Clinical implications
Nervous system	**Neuron** numbers lessened	Reduced memory, dementia
	Reaction time slower	Reduced balance and increased risk of falls
	Spinal cord neurons lost	
	Eyes: lens rigid and opaque	Cataract → reduced vision
	Ears: degeneration of cochlea	Loss of high-tone hearing
Endocrine system	Deterioration of beta-pancreatic cells → reduced insulin secretion	Impaired glucose tolerance
		? diabetes mellitus
	Reduced vitamin D function	Reduced Ca^{2+} in bone
	Reduced sex hormones	Changes in metabolism and physiological function
Gastrointestinal system	Reduced motility of gut	Constipation
	Weakened cardiac **sphincter**	Oesophageal reflux
Respiratory system	Reduced elasticity and increased rigidity of lungs and chest	Reduced lung function with activity and exercise
	Reduced **cough** and cilia function	Increased risk of infection
	Mismatch of ventilation/**perfusion**	Reduced oxygen saturation
Renal system	Nephron numbers down	Fluid balance impaired
	Glomerular filtration rate down	**Dehydration** or fluid overload risk
	Tubular function diminished	Drug excretion impaired
Cardiovascular system	Reduced maximum heart rate	Reduced exercise tolerance
	Aortic dilation	X-ray shows widened aortic arch
	Reduced elasticity of arteries	Postural **hypotension** more likely
	Reduced function sinoatrial node	Increased risk of atrial fibrillation
Musculoskeletal system	Reduced calcium in bones	Osteoporosis (↑ risk of **fractures**)
	Ageing changes in bone, cartilage, ligaments	Contribute to **osteoarthritis** development
	Vertebrae shrink	Loss of height
Skin	Photoageing	Skin disorders
	Atrophy, wrinkling, dryness	Cancers
	Decreased inflammatory response	Slow healing
Immune system	Reduced B- and T-cell **lymphocytes**	Increased vulnerability to **antigens** – new or previously encountered
	Reduced immune response	

Sources: Adapted from Blume-Peytavi et al., 2016; Colledge et al., 2010; De Tata, 2014; Loeser, 2010; Montecino-Rodriguez et al., 2013; Montero-Odasso and Duque, 2005.

Ageing, loneliness and social isolation

The risk of loneliness and social isolation are greater for older people as they are more likely to be living alone, living with a chronic condition or living away from family and friends. While loneliness and isolation are difficult to measure, they have a significant impact on both physical and psychological wellbeing (National Academies of Sciences, Engineering, and Medicine [NASEM], 2020). Loneliness has

been associated with higher risks of depression, anxiety and cardiac issues. Those living with heart failure are at an increased risk of death, hospitalisation or emergency admission (NASEM, 2020). Social isolation has been linked to a 50% increase in the risk of dementia and to an increased risk in premature deaths from a number of causes linked to physical inactively, frailty and lifestyle (NASEM, 2020). The ageing population were subject to extended periods of shielding and strict social isolation from family throughout the COVID-19 pandemic, the impact of which needs to be fully understood and incorporated in a person-centred approach to caring for older patient groups.

DIAGNOSIS OF DISEASE

A diagnosis is important because it enables provision of the correct treatment for the particular condition. The diagnosis is determined through:

- *History taking*: involves gaining information from the person and perhaps family members to help diagnosis by finding out as much as possible about the person and their condition, including factors which worsen or improve it, and the time-line of its development. In traumatic conditions, the history of the trauma is central to the direction of clinical thinking and is often provided by witnesses to the incident and emergency personnel.
- Active listening to the lived experience of the individual: How do the symptoms make them feel? How do they impact their lives? What, if any, treatments have they tried? Have they self-treated? What has worked and why?
- Physical examination, including:
  - *Signs*: are indicators of disordered function that can be readily observed: for example, rash or blue colouration of the skin, wheezing with respiration.
  - *Symptoms*: are indicators of disordered function that the person reports: for example, pain, pain on urination, confusion or loss of memory.
  - *Non-invasive tests*: there are a number of tests which can be carried out easily to aid diagnosis (Table 1.9).

Table 1.9 Examples of non-invasive tests for diagnosis

Measurement of physiological parameters	Vital signs (temperature, pulse, respiration rate)
	Blood pressure
	Respiratory function:
	SpO_2 (peripheral oxygen saturation)
	Respiratory volumes
Urine testing (clinical setting)	Glucose, **ketones**
	Protein
	pH
Microbiological testing	From secretions, wounds etc.
	Urine, sputum, faecal samples

In addition, a wide range of additional tests, many invasive in some degree, are carried out to assist or confirm diagnosis (Table 1.10). The key element in the process is to achieve the appropriate differential diagnosis, i.e. the correct diagnosis is identified through differentiating it from other conditions with similar signs and symptoms. A clear diagnosis carries with it information about the cause of the disease and recommended treatments.

Table 1.10 Types of additional tests for diagnosis

Haematological	Blood cells and proteins, antigens, blood types, etc.
Biochemical	Chemical/biochemical substances in body fluids and tissues
Cytological (biopsies)	Small samples of tissues for examination of cells
Microbiological	Infected tissues or exudate examined for identification of specific microbes
Radiological (X-rays) and other scans, e.g. MRI, ultrasound	Used to examine the structure of internal organs (e.g. bones, fetal development), soft tissues
Electrocardiograph (ECG)	ECG: electrical activity indicating function of the heart
Electroencephalograph (EEG)	EEG: electrical activity indicating function of the brain
Physiological	Tests of function of specific organs/systems, e.g. renal function
Endoscopies	Examining body cavities by insertion of flexible tube, often with a camera attached

Syndromes

A **syndrome** is a set of signs and symptoms that occur together and sometimes indicate a specific condition. In the past, a considerable number of these groups of signs and symptoms were named after the clinician who described them or the first person identified with the condition. The cause was often not known but the description has led to a hypothesis and guided research, which, with scientific developments, often result in identification of the cause and appropriate treatment. A wide range of syndromes occur that, between them, can affect every system of the body with a number of different causes: Table 1.11 identifies some examples.

Table 1.11 Examples of syndromes

Carpal tunnel syndrome	Tingling and numbness, followed by sudden, sharp, piercing pain through the wrist and up the arm
Chronic fatigue syndrome	Extreme, prolonged tiredness with muscle pain, memory problems, headaches, pain in multiple joints, sleep problems, sore throat and tender lymph nodes
Cushing's syndrome	Upper body obesity, thin arms and legs, fatigue and muscle weakness, hypertension, hyperglycaemia. Due to prolonged raised cortisol level
Down (or Down's) syndrome	Mental and physical disability, slow growth, characteristic facial features, may have other health problems, e.g. heart disease. Genetic disorder
Fetal alcohol syndrome	Physical abnormalities: wide-set and narrow eyes, growth problems, nervous system abnormalities. Behavioural difficulties: daily living, learning, emotions, etc.

(Continued)

Table 1.11 (Continued)

Marfan (or Marfan's) syndrome	Affects connective tissue, variable presentation. Often tall, thin and loose jointed, may have problems with heart and blood vessels, bones, eyes, skin, nervous system and lungs. Genetic disorder
Sudden infant death syndrome (SIDS)	'Cot death' – unexplained death during first year. Cause unknown but firm mattress and positioning on back for sleep reduces incidence
Sudden arrhythmic death syndrome (SADS)	Genetic heart conditions that can cause sudden death in apparently healthy people, often young and active

CHAPTER SUMMARY

This chapter provides an introduction to disease and the factors that influence the development and presentation of disorders. Individuals vary considerably both biologically and behaviourally and the variation that occurs influences how disease presents. You have learnt about the different types of disease and will be able to think about the implications for those with the different types of disorder and their families.

A number of the pathological mechanisms involved in the development of disease have also been considered. Among these, stress and ageing are major factors that influence disorders and how individuals and families respond. Understanding these is central to working with those requiring person-centred care.

Key points

- Individuals can vary in anatomy, physiology, biochemistry and development, resulting in differences in susceptibility to disease and how it presents. In addition, psychological/emotional responses and lifestyle behaviours also influence disease and the person-centred care required.
- Diseases can be acute, chronic or sub-acute, with differing disease pathways. In addition, someone with a chronic disorder can present with an acute exacerbation of their chronic illness. Diseases can also be congenital (i.e. existing from birth) or acquired (occurring after birth).
- Disease can be communicable (which can be passed onto someone else, e.g. infective) or non-communicable. In addition, there is a wide range of other causes of illness.
- There are a number of physiological mechanisms which influence disease presentation, including stress and ageing. Stress can present in an acute (Alarm Reaction) stage, in which changes are due to the action of catecholamine hormones, or a chronic state, resulting primarily from the action of glucocorticoid hormones. The changes that occur in ageing can also influence the body function and how disease presents. The body function and presentation of disease can also be impacted by the increased risk of loneliness and social isolation.
- Achieving an accurate diagnosis is essential for appropriate treatment. History, physical examination and a range of haematological, biochemical, radiological and other tests enable this to be achieved. A syndrome is a specific set of signs and symptoms.

Revise

Test your knowledge

Studying this chapter will have helped you to understand the causes of disease and, thus, identify the sorts of problems with which people in your care may need help. Revise the different sections in turn and then try to answer the questions below.

Answers are available online at **https://study.sagepub.com/essentialpatho2e/answers**.

1. Explain what you understand by 'normal' in relation to physical and behavioural function and how you can apply this understanding in providing high-quality care.
2. Describe five aspects of biological variation and how they vary in different individuals. Discuss the implications of these variations for planning and person-centred care.
3. Analyse and evaluate the implications for family-centred care of four aspects of behaviour that influence the development of chronic diseases.
4. State the main characteristics of each of the following categories of disease:
    i. Acute
    ii. Chronic
    iii. Sub-acute
    iv. 'Acute on chronic'
5. Differentiate between congenital and acquired disorders, and between communicable and non-communicable disease:
    i. Congenital
    ii. Acquired
    iii. Communicable
    iv. Non-communicable
6. Briefly explain, with examples, how disordered negative feedback can result in disease.
7. Describe the endocrine changes that occur in the acute stress response and evaluate their implications for the physiological changes in disease.
8. Identify the stages of the long-lasting stress response, the key physiological changes that occur and consider how you can plan family-centred care to facilitate quality of life.
9. What are the common effects of ageing on an individual's structure and function? How will these influence the development of physiological disorders as they age?
10. Discuss the importance of diagnosis and evaluate the contribution of the person's history, signs and symptoms, and additional tests in assisting diagnosis.

Revise

Ace your assessment

For additional revision resources visit **https://study.sagepub.com/essentialpatho2e**.

- Revise key terms relevant to this chapter with interactive flashcards.
- Test yourself with quizzes and multiple-choice questions.
- Access the glossary with audio to hear how complex terms are pronounced.

REFERENCES

American Heritage (2016) *Dictionary of the English Language*, 5th edition. Boston, MA: Houghton Mifflin Harcourt.

AVERT (2016) *Global Information and Education on HIV and AIDS*. Brighton, UK: AVERT. (Last full review: 1 December 2016.) Available at: www.avert.org/professionals/hiv-around-world/sub-saharan-africa/south-africa (accessed 29 May 2017).

Blume-Peytavi, U., Kottner, J., Sterry, W., Hodin, M.W., Griffiths, T.W., Watson, R.E.B. et al. (2016) Age-associated skin conditions and diseases: current perspectives and future options. *The Gerontologist*, *56* (Suppl 2): S230–42.

Bolton, D. and Gillett, G. (2019) *The Biopsychosocial Model of Health and Disease: New Philosophical and Scientific Developments*. London: Palgrave Macmillan.

Boore, J. (2000) Stress. In S.M. Hinchcliff, S.E. Montague and R. Watson (eds), *Physiology for Nursing Practice*, 2nd edition. Edinburgh: Harcourt Publishers.

Colledge, N.R., Walker, B.R. and Ralston, S.H. (2010) *Davidson's Principles and Practice of Medicine*, 21st edition. Edinburgh: Churchill Livingstone/Elsevier.

Collins English Dictionary (2012) *Complete and Unabridged Digital Edition*. London: HarperCollins Publishers.

Cook, N., Shepherd, A. and Boore, J. (2021) *Essentials of Anatomy and Physiology for Nursing Practice*, 2nd edition. London: Sage.

Cox, T. (1978) *Stress*. Basingstoke: Macmillan.

Daanen, H.A. and Van Marken Lichtenbelt, W.D. (2016) Human whole body cold adaptation. *Temperature*, *3* (1), 104–18. Available at: https://doi.org/10.1080/23328940.2015.1135688

De Tata, A. (2014) Age-related impairment of pancreatic beta-cell function: pathophysiological and cellular mechanisms. *Frontiers in Endocrinology* (online journal), *5* (Sept): article 138. Available at: www.ncbi.nlm.nih.gov/pmc/articles/PMC4153315/pdf/fendo- 05-00138.pdf (accessed 24 March 2016).

Deng, Y., Misselwitz, B., Dai, N. and Fox, M. (2015). Lactose intolerance in adults: biological mechanism and dietary management. *Nutrients*, *7* (9), 8020–35.

Engdahl, E., Gustafsson, R., Huang, J., Martin Biström, L.B., Stridh, P., Khademi, M. et al. (2019) Increased serological response against human herpesvirus 6A is associated with risk for multiple sclerosis. *Frontiers in Immunology*, *10* (Article 2715). https://doi.org/10.3389/fimmu.2019.02715

Engel, G.L. (1977). The need for a new medical model: a challenge for biomedicine. *Science*, *196* (4286): 129–36.

Foster F. and Collard M. (2013) A reassessment of Bergmann's rule in modern humans. *PLoS One*, *8* (8): e72269. doi: 10.1371/journal.pone.0072269. PMID: 24015229; PMCID: PMC3756069

Huovinen, E., Kaprio, J., Laitinen, L.A. and Koskenvuo, M. (1999) Incidence and prevalence of asthma among adult Finnish men and women of the Finnish twin cohort from 1975 to 1990, and their relation to hay fever and chronic bronchitis. *Chest*, *115* (4): 928–36.

Lloyd, C., Smith, J. and Weinger, K. (2005) Stress and diabetes: a review of the links. *Diabetes Spectrum*, *18* (2).

Loeser, R.F. (2010) Age-related changes in the musculoskeletal system and the development of osteoarthritis. *Clinics in Geriatric Medicine*, *26* (3): 371–86.

McBride, W.G. (1961) Thalidomide and congenital abnormalities (Letter to the Editor). *The Lancet*, *278* (7216): 1358.

McCormack, B. and McCance, T. (2021) The person-centred nursing framework. In J. Dewing, B. McCormack and T. McCance (eds), *Person-centred Nursing Research: Methodology, Methods and Outcomes*. New York, NY: Springer, pp. 13–22.

Montecino-Rodriguez, E., Berent-Maoz, B. and Dorshkind, K. (2013) Causes, consequences, and reversal of immune system ageing. *Journal of Clinical Investigation*, *123* (3): 958–65.

Montero-Odasso, M. and Duque, G. (2005) Vitamin D in the aging musculoskeletal system: an authentic strength preserving hormone. *Molecular Aspects of Medicine*, *26*: 203–19.

National Academies of Sciences, Engineering, and Medicine (2020) *Social Isolation and Loneliness in Older Adults: Opportunities for the Health Care System*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25663external icon

Overfield, T. (2017) *Biologic Variation in Health and Illness: Race, Age and Sex Differences*, 2nd edition. Menlo Park, CA: Addison-Wesley.

Selye, H. (1976, reissued 1978) *The Stress of Life*. New York: McGraw-Hill.

Shikova, E., Reshkova, V., Kumanova, A., Raleva, S., Alexandro, D., Capo, N. et al. (2020) Cytomegalovirus, Epstein-Barr virus, and human herpesvirus-6 infections in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Journal of Medical Virology*, *92* (12): 3682–8. https://doi.org/10.1002/jmv.25744

van den Beld, A.W., Kaufman, J.M., Zillikens, M.C., Lamberts, S., Egan, J.M., & van der Lely, A.J. (2018). The physiology of endocrine systems with ageing. *The Lancet. Diabetes & Endocrinology*, *6* (8): 647–58. https://doi.org/10.1016/S2213-8587(18)30026-3

Wang, C.H., Wu, S-B., Wu, Y-T. and Wei, Y-H. (2013) Oxidative stress response elicited by mitochondrial dysfunction: implication in the pathophysiology of aging. *Experimental Biology and Medicine*, *238* (5): 450–60.

Wang, M., Gong, W., Hu, R., Pan, J., Lv, J., Guo, Y. et al. (2019) Associations between stressful life events and diabetes: findings from the China Kadoorie Biobank study of 500,000 adults. *Journal of Diabetes Investigation*, *10* (5): 1215–22. http://doi.org/10.1111/jdi.13028

Williams, E.D., Magliano, D.J., Tapp, R.J. et al. (2013) Psychosocial stress predicts abnormal glucose metabolism: the Australian diabetes, obesity and lifestyle (AusDiab) study. Annals of Behavioral Medicine, *46*: 62–72. https://doi.org/10.1007/s12160-013-9473-y

World Health Organisation (WHO) (1948) Preamble to the Constitution of WHO as adopted by the International Health Conference, New York, 19 June–22 July 1946; signed on 22 July 1946 by the representatives of 61 States. Official Records of WHO, no. 2, p. 100. Entered into force on 7 April 1948. (Note: The definition has not been amended since 1948.)

World Health Organisation (WHO) (2018) *Health Topics: Disabilities*. Geneva: WHO.

World Health Organisation (WHO) Europe (2016) *Health Topics: Noncommunicable Diseases*. Copenhagen, Denmark: World Health Organisation Regional Office for Europe. Available at: www.euro.who.int/en/health-topics/noncommunicable-diseases/noncommunicable-diseases