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Stress, the Immune System, and Healthy Ageing

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Introduction

The stress response in humans, although an adaptive mechanism initially, has the potential to be chronic and detrimental to the organism if too large and/or prolonged (Sapolsky 2007). This particularly seems to be the case later in the lifespan; in fact, although ageing is a physiological process that is part of normal development (Cutler 1991a, b), some of the changes in older age mirror the chronic effects of psychological stress on several of the body's biological systems. This chapter mainly focuses on the impact of stress on the immune system and the implications for health in older age, as stress effects on all bodily systems are beyond the scope of one chapter. Further, as the immune system undergoes several changes with ageing, this results in increased susceptibility to infectious diseases, all of which are also influenced by stress. The chapter begins

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with an introduction to psychological stress and its relationship to illness susceptibility and a summary of the physiological responses to stress. It then provides an introduction to the immune system and the effects of ageing on it, including the impacts of ageing on stress hormones. Following this background, the chapter examines research evidence in this area, focusing on the potentially negative impacts of caregiver stress on immunity in ageing and the potentially positive impacts of social support.

Psychological Stress

Psychological stress can be characterised in a number of ways but is usually considered as something that exceeds our coping abilities (Lazarus and Folkman 1984). One way of characterising psychological stress in order to understand its sources is to categorise it as cataclysmic events, stressful life events, or daily hassles. Cataclysmic events include natural disasters and war which can have considerable effects on health. One example would be the impact of being a soldier during the Vietnam War, which led to the development of post-traumatic stress disorder (PTSD) in many veterans, although not all. Those veterans who developed PTSD were then at increased risk of a range of non-communicable diseases over the next 20 years compared to those who did not respond to the stress or war with PTSD (Boscarino 1997). Stressful life events are occurrences that happen to most individuals but not necessarily regularly, and their impact can be months to years such as unemployment, bereavement, marriage/divorce/separation, and caregiving for a spouse or family member. An example of the impact of this type of stressor is illustrated in a study in which individuals who had suffered more stressful life events and generally felt more stressed were more susceptible to developing an upper respiratory tract infection after exposure to a rhinovirus (such as a common cold) than those who reported fewer stressful events and lower stress levels (Cohen et al. 1991). The final category of stressful daily hassles includes a range of generally short-lived minor inconveniences such as misplacing something or being late. Such hassles are common and regular but can also relate to health outcomes, particularly in the case of a

build-up of many hassles over a short time period. For example, individuals who reported higher numbers of minor daily hassles on a particular day showed increased symptoms of malaise and illness four days later (Sheffield et al. 1996). Psychological stress can also be characterised as of different durations; acute stress lasts for minutes or hours whereas chronic stress lasts for days, weeks, months, or even years, and the resultant physiological impacts on health differ considerably, as is discussed in the next section.

The Stress Response

The physiological response to psychological stress was characterised by Walter Cannon (1929) as the 'fight or flight' response. The main function of this response is to maintain bodily homoeostasis. Biologically, the key site involved in this process is the hypothalamus (Barrett 2005), a part of the brain that communicates by sending nerve impulses to other parts of the body. In this way, the hypothalamus acts within seconds and via the sympathetic nervous system stimulates the medulla of the adrenal gland to release catecholamines (adrenalin and noradrenalin) which act on receptors throughout the body to result in several effects such as increased heart rate, blood pressure, and respiration; activation of smooth muscle; and increased core temperature and pain threshold (Charmandari et al. 2005). In addition, the hypothalamus also produces chemical messengers that act more slowly and in the next minutes travel through the hypothalamic-pituitary-adrenal (HPA) axis (Sapolsky et al. 2000). Chemical messengers in this pathway include corticotrophin releasing hormone (CRH) which stimulates the anterior pituitary gland to release another hormone, adrenocorticotropic hormone (ACTH), into circulation. The target organ of ACTH is again the adrenal gland, but this time stimulates the cortical cells that synthesise and release species-specific glucocorticoids (GC) into the blood. The tight control of these GC (mainly cortisol in humans) is sustained via negative feedback that controls and terminates the release of CRH (Griffin and Ojeda 2004). Cortisol potentiates the effects of catecholamines within the body (Charmandari et al. 2005) as well as initially activating the immune

system, then later working as an anti-inflammatory agent generally suppressing immune function, to prevent harmful over-activation (Munck et al. 1984). However, when stress is prolonged, chronic, or there are repeated exposures to stressful events, this puts the body out of homoeostasis for too long and dysregulation of the stress response axis can occur resulting in detrimental effects throughout the body, for example, on the cardiovascular system (McEwen 1998; Phillips 2011; Sedova et al. 2004) and also by suppression of the immune system (Sorrells and Sapolsky 2007). Acute stress can in fact be beneficial for the immune system, leading to temporary upregulation of immune cells responses, and has been associated in some cases with improved antibody responses to vaccination, for example (Edwards et al. 2006). In contrast, chronic stress, such as caregiving for a child with developmental delay, has been shown to down-regulate immunity, resulting in a decrease in the antibody response to vaccination, for example (Gallagher et al. 2009a).

The Immune System

The immune system can be considered as two distinct but interconnected elements: the innate and the adaptive immune systems. The innate response is often referred to as the 'first line of defence' against infection as it comprises mechanisms that are the first to react to an infection. The adaptive immune system is slower to respond but has the advantages that it includes memory of pathogens encountered and that its response is specific for each pathogen, thus conferring a tailored and long lasting protection against further infection by the same pathogen. The innate immune system consists of soluble components, namely the complement system, which consists of a series of proteins in the blood which, when activated, stimulate, or complement, the work of the cellular elements. The cellular elements, including neutrophils which deal with rapidly dividing bacteria and fungi, eosinophils which respond to parasitic infections, macrophages which secrete soluble factors (such as the cytokines TNFα, IL-1, IL-6) to co-ordinate and amplify the immune response and also provide immunity against intracellular bacteria, and Natural Killer (NK) cells which detect and kill virally infected cells and tumour cells.

Adaptive immunity is provided by T and B lymphocytes, which develop and mature in the thymus and bone marrow respectively. T cells can be further classified into CD4 expressing helper cells (which in turn can be split into Th1 and Th2 types), CD8 expressing cytotoxic cells, and CD25 expressing T regulatory cells, which have immune suppressive function. B cells, when presented with an antigen (by dendritic cells or with T cell help) produce antibodies to provide extended protection against infections. When a naïve T or B cell encounters a pathogen it will proliferate and differentiate into an effector cell or a memory cell, so that if the pathogen is encountered a second time a more rapid response can be achieved. Ageing is known to have deleterious effects upon both the innate and adaptive immune responses, though the latter is much better characterised (Phillips et al. 2007).

Ageing and Immunity

With ageing, the innate immune response goes through some changes. For example, complement activation appears to be unaffected, but neutrophil bactericidal and phagocytic function in vitro is dramatically reduced (Butcher et al. 2001). Macrophage function is also modified, although the literature is rather contradictory, including reports of reduced capacity to engulf pathogens, release chemicals such as superoxides to kill pathogens, as seen in neutrophils, but enhanced secretion of the cytokines IL-6 and IL-8 in response to pathogens. NK cells are also affected by ageing; while their numbers do not change with age, their cytotoxic capacity is reduced (Hazeldine et al. 2012) which has also been shown to relate to reduced survival in people aged over 75 years (Ogata et al. 2001). In the adaptive immune system, the thymus gland atrophies and thus fewer naïve T cells are produced. As the size of the T cell pool is maintained at a constant level, the proportion of T cells that are memory cells increases. Consequently, as we age, we are less able to deal with new pathogens. In addition to changes in the ratio of naïve to memory T cells, there is a shift from T-helper 1 to T-helper 2 cells, and the end result is reduced cell-mediated, Th1-type, immunity. Finally, with ageing, antibody production in response to antigen declines; for example,

older people produce a lower antibody titre (a measure of how much antibody a person has produced) in response to vaccination than younger individuals and the antibodies produced are of lower affinity (binds less well to the invading antigens). This is thought to be largely the result of a decline in T cell help for B cells in older adults.

Another concept that frequently appears in the literature when discussing the ageing of the immune system is inflammaging (Franceschi et al. 2007). Inflammatory factors are damaging in excessive amounts and inflammaging indicates an imbalance between inflammatory factors necessary to fight the infection and anti-inflammatory components that act as a counter weight. It has been suggested that ageing and longevity could, therefore, potentially be dependent on this balance (Franceschi et al. 2007). This would mean that immunosenescence, together with inflammatory markers such as different cytokines (IL-6, IL-8, and IL-15), could contribute to the prediction predictors of the longevity of organisms.

Stress Hormones and Ageing

As outlined earlier, stress, whether physical or psychological, is broadly sensed by two systems within the hypothalamus, the HPA axis and the sympathetic-adrenal-medullary system. Stress induces the release of catecholamines from the adrenal medulla and both cortisol and dehydroepiandrosterone (DHEA) from the adrenal cortex. Catecholamines and cortisol can both be immunosuppressive if chronically elevated. In contrast, DHEA is a precursor to sex hormones and is considered to be immune enhancing (Butcher et al. 2005). Due to the impact of these hormones on immunity, any change in their production could therefore have significant health implications. In humans, the production of DHEA and its sulphated form, DHEAS, declines with age, a process termed the adrenopause (Orentreich et al. 1984). The synthesis of DHEA is maximal in humans at age 20–30 and declines gradually thereafter, so that by the seventh decade levels of DHEA can be as low as 10% of that seen in young adulthood (Orentreich et al. 1992); this adrenopause occurs at similar rates in both males and females. However,

although DHEA/S levels fall with age, the production of glucocorticoids such as cortisol is remarkably unaltered (Orentreich et al. 1992), resulting in a relative excess of cortisol over DHEA/S and an imbalance of immune suppression over immune enhancement. The age-related immunological and endocrinological changes outlined earlier may have implications for the ability to cope (physiologically) with stress in older adults. It is likely that the combination of adrenopause, leading to a relative preponderance of cortisol, and an already reduced immune defence against infection through immune senescence, may leave this population particularly vulnerable to the negative effects of stress on immunity (Graham et al. 2006; Phillips et al. 2007). However, younger adults are also susceptible to the impact of stress on immunity. For example, various studies have now shown reduced antibody responses to vaccination in those with greater self-reported stress levels (Burns et al. 2003; Phillips et al. 2005). Nonetheless, when ageing is combined with stress, the effects on immunity are often more detrimental. For example, in one large study, caregivers, but only those aged over 60 years, showed lower levels of a particular antibody, salivary immunoglobulin A, which targets pathogens in biological fluids, particularly saliva at mucosal surfaces (Gallagher et al. 2008a).

Caregiver Stress and Immunity in Ageing

As indicated earlier, one commonly studied model of the impact of stress on immunity is the role of caregiving for another person, be it a spouse or child with a physical or mental illness or disability. Older caregivers have most commonly been studied in this context, using the model of family dementia caregiving (Gouin et al. 2008). Caregiving is now well established as having a serious effect on psychological wellbeing and physical health among caregivers when compared to matched non-caregiving individuals (Pinquart and Sorensen 2003). Both innate and adaptive immunity are affected by chronic stress experienced by older adults. For example, wound healing was slower in older dementia caregivers when compared to age, sex, and income-matched controls (Kiecolt-Glaser et al. 1995). Further, lower production of proinflammatory

cytokines involved in the wound healing process such as IL-1α, IL-8 (Glaser et al. 1999), as well as IL-1β (Kiecolt-Glaser et al. 1995) has been observed in caregivers compared to controls. NK cells are essential in targeting tumour or virally infected cells. (Esterling et al. (1994) showed that NK cells from caregivers respond more weakly compared to NK cells from controls.)

A further association with the chronic stress of caregiving was found for adaptive cell-mediated immunity; elevated cortisol levels as well as poorer proliferation to antigen and lower IL-2 production was shown in a caregiving group (Bauer et al. 2000). Caregiving stress in older adults has also been shown to be associated with the T-helper 1 to T-helper 2 shift in the type of cytokine responses, with the difference that in older stressed individuals this was driven purely by an increase in IL-10 production, with no difference in IFN-γ production by Th1 cells (Glaser et al. 2001). It is likely that stress-induced changes in catecholamine levels (Elenkov and Chrousos 2002) during the psychological stress response drive this cytokine-related behaviour.

Inflammaging, as observed in older adults, might also be more severe among chronically stressed older adults, such as dementia caregivers. Indeed, when compared to non-caregiving older adults who also had immunosenescence, not only did older caregivers show higher levels of IL-6 (von Kanel et al. 2006) but its rate of increase was four times higher than in non-caregiving older controls, leaving them particularly vulnerable to IL-6 related diseases such as frailty, cardiovascular diseases, osteoporosis, and others (Ershler and Keller 2000).

A novel approach for assessing the severity by which caregiving stress affects the immune system of older caregivers is that of studies of latent-virus antibody titres. It is known, for example, that reactivation of latent viral infections, such as those initiated by the Herpes group (HSV-1, EBV, and CMV) is typical for immunosuppressed patients such as HIV and transplant patients (Rasmussen 1991). Interestingly, older spousal caregivers had higher IgG antibody titres against EBV VCA (virus capsid antigen) compared to the matched controls, indicating poorer control of the latent infection in this group (Kiecolt-Glaser et al. 1991). Together with the higher antibody titre to total viral antigen of HSV-1, caregivers also had a decreased virus-specific T cell response; another component of

immune system necessary for controlling the infection (Glaser and Kiecolt-Glaser 1997). Older caregivers have also been characterised by higher antibody titres against CMV when compared to the controls (Pariante et al. 1997). In this instance, showing higher antibody levels against CMV is an indicator that the virus is not under control and therefore indicates poorer immunity.

Vaccination responses are affected by increasing age which makes older adults particularly vulnerable to frequent infections such as pneumonia and influenza, among the top five causes of high morbidity and mortality in this age group (Thompson et al. 2003). It would be expected that this aspect of immune incompetence would be further exacerbated in older adults affected by the chronic stress of caregiving. This is indeed the case; a significantly lower percentage of older caregivers of dementia patients showed a four-fold increase in antibody titre in response to vaccination against the influenza virus, a response that is clinically considered to be protective against infection (Vedhara et al. 1999a). This was accompanied by higher salivary cortisol concentration in the caregiver group when compared to the controls, pointing again to the role of HPA axis in immune regulation among chronically stressed individuals. Most antigens, however, trigger both humoral, that is, the antibody response which is generated by B lymphocytes, as well as cellular responses, mainly mediated by cytotoxic CD8+ T cells (Glaser et al. 2000; Kiecolt-Glaser et al. 1996; Siergist 2008). In addition, CD4+ helper T cells are necessary as mediators between those two. It has been shown that both the antibody response to medical vaccination against the influenza virus, as well as IL-2 production in response to antigen stimulation, was lower in caregivers comparing to the controls (Kiecolt-Glaser et al. 1996). In the case of the pneumococcal pneumonia vaccine, even though caregivers managed to exert an adequate immune response initially, shown as a rise in IgG antibody titre, it declined over time more rapidly in this group than in the group of matched controls, likely either as a consequence of decrease in number of antibody-specific B cells, or their ability to produce antibody (Glaser et al. 2000; Vedhara et al. 1999a). However, this impact of caregiving stress on vaccination responses is not unique to older caregivers as was previously thought (Vedhara et al. 2002). One elegant study showed that if the caregiving stress is severe enough, particularly if the

behaviours exhibited by the care recipient are challenging, then even younger caregivers can display decrements in the antibody response to vaccination. This was shown in young parental caregivers of children with a learning delay such as autism, Down's Syndrome, and other less well-known syndromes, in comparison to parents of typically developing children. Parental caregivers showed a reduction in the production of antibodies to the influenza and pneumococcal vaccinations, and this was particularly marked among those whose children displayed severe challenging behaviours (Gallagher et al. 2009a, b). However, it should be noted that there was a trend for an effect for ageing such that the lowest antibody titres were among parental caregivers at the older end of the age group (Gallagher et al. 2009a). These studies have been followed up with similar case-control design studies but including both younger and older adults to examine the interaction between ageing and caregiving stress. These studies showed that for some aspects of immunity, ageing or the interaction between stress and ageing were not the key predictors of poorer immune function, but the stress itself was. In these studies caregivers reporting higher psychological distress (depression, anxiety, and caregiving burden) showed the poorest neutrophil function independent of age (Vitlic et al. 2015), and individuals with higher levels of psychological distress generally also displayed a somewhat higher cortisol:DHEAS ratio within each age group (Vitlic et al. unpublished data).

Chronic Stress and Immunity in Ageing

Given the importance of the caregiving model of stress, little attention has been given to other sources of stress among older adults and immunity. Although one study has reported that perceived stress, measured using the perceived stress questionnaire (Cohen et al. 1983), was associated with a poorer antibody response to the influenza vaccine in older adults (Kohut et al. 2002), another small-scale study found no association between perceived stress and antibody status following this vaccination in very old (mean age 84 years) nursing home residents (Moynihan et al. 2004). Very few studies have focused on stressful life events, despite these being a common means of assessing the impact of stress on

immunity in younger samples (e.g., Burns et al. 2003; Phillips et al. 2005). However, a study published in 2006 examined overall stressful life events using a life events rating scale and showed that middle-aged and older adults with higher ratings of stress and disruptiveness for the stressful events they had experienced in the past two years showed lower levels of IgA in saliva (Phillips et al. 2006b). Further, another study took advantage of the UK National Health Service vaccination programme whereby adults aged 65+ years are invited for an annual influenza vaccination. Stressful life events and social support were measured using standardised psychometric questionnaires and antibody titres were assessed at baseline prior to vaccination and one month later. Although there was no overall effect of stress and social support, one particular stressor of import to older adults related to their immune responses; those who had suffered bereavement in the past year showed lower antibody titres to two of the three 'flu vaccine components' (Phillips et al. 2006a). The absence of an association between overall life events and antibody response to influenza vaccination in the older adults and vaccination study (Phillips et al. 2006a) contrasts with the results of previous research on young participants (Burns et al. 2003; Phillips et al. 2005). However, in these student studies, the modal number of life events experienced in the past year was six, with no participants reporting one or less events (Phillips et al. 2005), whereas in the older sample, the modal number of major life events in the year prior to vaccination was zero, with 31% of the sample reporting no events and a further 17% reporting only one. This might be due to differences between student and older adult life event stress scales. In the student studies, less serious events were included in the stress scale, for example, getting an unjustified low mark on a test or minor financial problems, along with more major events, whereas the older adults' life events scale tended to focus on exposure to major life events. Accordingly, the absence of an association between antibody response and overall life events in older adults may reflect the use of a scale including only serious, rarer life events. However, the results for bereavement would argue against this explanation. In addition, it is also possible that older people simply experience fewer general life events than younger samples. There is certainly evidence to this effect: older individuals encountered fewer major life events than middle-aged participants in a large cohort study in the

west of Scotland using the same life events measure as the Phillips et al. (2006a, b) study, but retrospectively over two years. Middle-aged (mean age 44 years) participants identified a mean of 2.0 events whereas the mean number of events for the older group (mean age 63 years) was 1.7 (Carroll et al. 2005). These data also suggest that the Phillips et al. (2006a, b) participants were not unusual in experiencing few life events, given that the mean number of events reported over one year was 2.9. Accordingly, it may be that individual differences in general life events exposure are less important for immunity as people age, whereas bereavement, a specific life event that older people are more likely to encounter than the young, assumes greater prominence.

The negative association between bereavement and antibody status following vaccination is in line with previous studies of bereavement and immune function. Bereavement has been associated with in vitro functional immune measures such as decreased natural killer cell cytotoxicity and poorer lymphocyte proliferation to antigen (Bartrop et al. 1977; Goodkin et al. 1996; Irwin et al. 1987; Kemeny et al. 1995; Schleifer et al. 1983; Zisook et al. 1994). In follow-up work, focussing on the two-month period post-bereavement, it was shown that neutrophils' killing ability was suppressed in bereaved older adults, an effect that was accompanied by the increase in cortisol:DHEAS ratio (Khanfer et al. 2011). However, when this study was replicated and also included younger adults, the impact of bereavement stress on neutrophil function was only evident for older caregivers (Vitlic et al. 2014). Previous work has suggested that psychological morbidity may be a mediator between the bereavement and both immune system effects and their impact on risk of morbidities such as influenza and pneumonia. For example, Zisook et al. (1994) reported an effect on immune indices where the bereaved older adults were reporting more depressive symptoms Other work has indicated that the influence of conjugal bereavement on mortality is modified by gender, existing cardiovascular disease status, and depression (Stahl et al. 2016).

Stress need not be only psychological stress but could also be physiological stress such as physical disease or physical trauma such as a severe fracture or burn. Older adults who experienced the physical trauma or stress of hip fracture had higher cortisol:DHEA ratios than healthy

controls and lower neutrophil function (Butcher et al. 2005), and individuals with lower neutrophil function were more likely to succumb to infection post-fracture (Butcher et al. 2003). Further, older adults who developed depression post-hip fracture showed the highest cortisol:DHEA ratio and poorest neutrophil function (Duggal et al. 2013), as well as worse frailty and slower physical recovery (Phillips et al. 2013).

Social Support and Immunity in Ageing

Given the substantial impact of various types of stress on immunity in older adults, as outlined earlier, understanding psychological factors that can help to enhance or improve immunity in this group is particularly important. Social support, or comfort, caring, esteem, or help provided by other people or social groups can be a key resource that helps individuals cope with life. It has also been shown to have a substantial impact on health; for example, individuals with low numbers of supportive relationships had two to three times the mortality risk compared to those with large social networks (Berkman and Syme 1979). Indeed, social network size and quality and frequency of social support have been shown to impact on morbidity and mortality from serious diseases in many epidemiological studies, for example (Barger 2013; House et al. 1982; Kaplan et al. 1988). Social support has also been shown to relate to immune function. For example, whereas students who had seroconverted (developed antibodies) after the first injection of the standard three-dose hepatitis B vaccination were less anxious and reported lower stress levels than those who had not, those who reported greater social support demonstrated a stronger combined immune response to the booster third inoculation (Glaser et al. 1992). In another study of college first-year students, loneliness and smaller social network size were associated with a poorer antibody response to the A/New Caledonian strain of the influenza vaccination (Pressman et al. 2005). Finally, higher social support scores, particularly higher frequency of tangible support, were related to an increased antibody response to the A/Panama component of the influenza vaccination, again in university students (Phillips et al. 2005).

In a study of social support in older adults, social support was negatively correlated with A/Panama influenza strain antibody status following vaccination, a finding which contradicts the studies with students above that even the authors found difficult to explain (Moynihan et al. 2004). In contrast, a larger study of older adults considered the actual vaccination response, that is, the change in antibody levels from pre- to post-vaccination (Phillips et al. 2006a). In this study, although social network size and functional social support were not related to antibody response, married/cohabiting participants showed a better antibody response to the A/Panama strain at one month than those who were not married, particularly widowed, participants. Also, for those who were married or cohabiting, higher marital satisfaction was related to higher titres to A/Panama at one month. This is not entirely surprising given that poorer marital quality, in terms of adjustment and negative marital interactions, is associated with inferior functional immunity evidenced through reduced proliferation to some antigens, poorer latent virus control (Kiecolt-Glaser et al. 1987, 1997, 1988, 1993), and weaker NK cell cytotoxicity (Miller et al. 1999) in the general population. Further, it is possible that the variations between older caregivers and controls in terms of vaccination response (Glaser et al. 1998, 2000; Kiecolt-Glaser et al. 1996; Vedhara et al. 1999b) may be driven, at least in part, by the effects of caregiving on marital quality and satisfaction, although more specific measurement of stressful life events and marital parameters would be necessary to support this speculation. Whatever the case, these findings resonate with the broad consensus that both marriage (Gordon and Rosenthal 1995; House et al. 1988; Johnson et al. 2000; Verbrugge 1979) and marital satisfaction (Coyne and DeLongis 1986; Kiecolt-Glaser and Newton 2001; Robles and Kiecolt-Glaser 2003) are beneficial for health. Further, it is possible that in an older aged population, general social support is less critical, whereas the specific social support resource of a happy marriage becomes more important for health, including susceptibility to infection.

Interestingly, the studies of social support and immunity show direct associations rather than an effect of social support via buffering the negative impact of stress. It is possible that for psychological and other health outcomes, social support can buffer stress effects (Lazarus and Folkman

1984; Rosengren et al. 1993), whereas for immune function, social support might impact immunity independently. Certainly, social support has been shown to affect different types of vaccination responses to those impacted by stressful life events in various studies among younger adults (Gallagher et al. 2007, 2008b; Phillips et al. 2005).

Conclusion

This chapter has focused on the impact of ageing on stress hormones and immune function as well as the effects of stress on immunity and the role of stress hormones. It also briefly touched on a variable that is known to relate to stress often, social support, and its links with immune function in ageing. Ageing is considered as a normal process, but in some cases the normal processes of ageing (adrenopause, inflammaging, immune senescence) can contribute to a reduced ability to deal physiologically with stress in later life. However, the research has also shown that stress can impact on stress hormone levels and certain aspects of immunity even in young healthy adults; thus, chronic stress throughout the life span will likely further impact on health and wellbeing as these individuals age. Consequently, individuals with a life history of fewer severe stress exposures may be at lower risk of a heightened cortisol:DHEA ratio, immune decrements, and greater inflammation, even in the presence of the normal hormonal and immune changes associated with ageing. These individuals are thus likely to be more resilient to stress or trauma if and when it does occur later in the lifespan, although longitudinal research would be needed to confirm this possibility.

Although avoiding stressful events themselves may not be a realistic undertaking for most individuals, certainly where stress levels can be reduced by healthy behaviours or seeking social support, these methods are likely to have positive psychological, immune, and thus health impact throughout life, not just in older age. Healthy behaviours with direct effects on both perceived stress levels and immune function can also be pursued in order to increase resilience in later life. These would include exercise or physical activity, adequate sleep, a balanced diet, not smoking or taking drugs, and moderation of alcohol intake, some of which is

outlined in Chapter 6, but their effects on immunity and within healthy ageing warrant a separate chapter each.

A certain level of stress can be beneficial for health and indeed the immune system. As described in this chapter, this occurs in the case of acute stress, where the immune system can demonstrate enhanced function in response in much the same way a vaccine challenges the immune system (Lewitus and Schwartz 2009). The challenge for healthy ageing is for the occurrence of acute stressors not to escalate to the extent where they lead to overload and individuals beginning to show the detrimental physiological effects of chronic stress.

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